

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
8 August 2002 (08.08.2002)

PCT

(10) International Publication Number
WO 02/060317 A2

(51) International Patent Classification⁷: A61B Avenue N.E., Seattle, WA 98125 (US). JIANG, Yuqiu [CN/US]; 5001 S. 232nd Street, Kent, WA 98032 (US).

(21) International Application Number: PCT/US02/02781

(74) Agents: CHRISTIANSEN, William, T.; Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 et al. (US).

(22) International Filing Date: 30 January 2002 (30.01.2002)

**COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF
PANCREATIC CANCER**

STATEMENT REGARDING SEQUENCE LISTING

5

The Sequence Listing associated with this application is provided on CD-ROM in lieu of a paper copy under AI § 801(a), and is hereby incorporated by reference into the specification. Four CD-ROMs are provided containing identical copies of the sequence listing: CD-ROM No. 1 is labeled "COPY 1 – SEQUENCE LISTING PART," contains the file 566pc.app which is 2.9 MB and created on 30 January 2002; CD-ROM No.2 is labeled "COPY 2 – SEQUENCE LISTING PART," contains the file 566pc.app which is 2.9 MB and created on 30 January 2002; CD-ROM No. 3 is labeled "COPY 3 – SEQUENCE LISTING PART," contains the file 566pc.app which is 2.9 MB and created on 30 January 2002; CD-ROM No. 4 is labeled "CRF," 10 contains the file 566pc.app which is 2.9 MB and created on 30 January 2002; 15 contains the file 566pc.app which is 2.9 MB and created on 30 January 2002.

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates generally to therapy and diagnosis of cancer, such as pancreatic cancer. The invention is more specifically related to polypeptides, comprising at least a portion of a pancreatic tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides are useful in pharmaceutical compositions, e.g., vaccines, and other compositions for the diagnosis and treatment of pancreatic cancer.

25

Description of the Related Art.

Cancer is a significant health problem throughout the world. Although advances have been made in detection and therapy of cancer, no vaccine or other universally successful method for prevention and/or treatment is currently available. 30 Current therapies, which are generally based on a combination of chemotherapy or surgery and radiation, continue to prove inadequate in many patients.

Pancreatic cancer is the fifth leading cause of cancer death in the United States. Current therapies for this common and difficult-to-treat disease include surgery and/or chemotherapy. Although 5-year survival rates after surgical removal of the pancreas and a large portion of the duodenum have improved, the procedure is only used on 9% of patients. Of these, the highest reported 5-year survival rate is in the range of 20%. Patients with advanced pancreatic cancer are treated primarily by chemotherapy. The objective of such therapy is to prolong patient survival. Surgery and irradiation are used as well to relieve pain and reduce organ blockage.

In spite of considerable research, pancreatic cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

BRIEF SUMMARY OF THE INVENTION

In one aspect, the present invention provides polynucleotide compositions comprising a sequence selected from the group consisting of:

- (a) sequences provided in SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550;
- (b) complements of the sequences provided in SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550;
- (c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550;
- (d) sequences that hybridize to a sequence provided in SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550, under moderately stringent conditions;
- (e) sequences having at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identity to a sequence of SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550;
- (f) sequences having at least 90% identity to a sequence of SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550; and

(g) degenerate variants of a sequence provided in SEQ ID NOS:1-66, 75-152, 174-177, 182, 184-452, and 454-4550.

In one preferred embodiment, the polynucleotide compositions of the 5 invention are expressed in at least about 20%, more preferably in at least about 30%, and most preferably in at least about 50% of pancreatic tumor samples tested, at a level that is at least about 2-fold, preferably at least about 5-fold, and most preferably at least about 10-fold higher than that for normal tissues.

The present invention, in another aspect, provides polypeptide 10 compositions comprising an amino acid sequence that is encoded by a polynucleotide sequence described above.

The present invention further provides polypeptide compositions comprising an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NOS:67-74, 153-173, 178-181, 183, 453, 4551-4554, 4558-4560.

15 In certain preferred embodiments, the polypeptides and/or polynucleotides of the present invention are immunogenic, *i.e.*, they are capable of eliciting an immune response, particularly a humoral and/or cellular immune response, as further described herein.

The present invention further provides fragments, variants and/or 20 derivatives of the disclosed polypeptide and/or polynucleotide sequences, wherein the fragments, variants and/or derivatives preferably have a level of immunogenic activity of at least about 50%, preferably at least about 70% and more preferably at least about 90% of the level of immunogenic activity of a polypeptide sequence set forth in SEQ ID NOS:67-74, 153-173, 178-181, 183, 453, 4551-4554, 4558-4560 or a polypeptide 25 sequence encoded by a polynucleotide sequence set forth in SEQ ID NOS:1-66, 75-152, 174-177, 182, 184-452, and 454-4550.

The present invention further provides polynucleotides that encode a polypeptide described above, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

5 Within a related aspect of the present invention, the pharmaceutical compositions, e.g., vaccine compositions, are provided for prophylactic or therapeutic applications. Such compositions generally comprise an immunogenic polypeptide or polynucleotide of the invention and an immunostimulant, such as an adjuvant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to
10 a polypeptide of the present invention, or a fragment thereof; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Illustrative
15 antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, pharmaceutical compositions are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

20 The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins, typically in the form of pharmaceutical compositions, e.g., vaccine compositions, comprising a physiologically acceptable carrier and/or an immunostimulant. The fusions proteins may comprise multiple immunogenic
25 polypeptides or portions/variants thereof, as described herein, and may further comprise one or more polypeptide segments for facilitating the expression, purification and/or immunogenicity of the polypeptide(s).

Within further aspects, the present invention provides methods for stimulating an immune response in a patient, preferably a T cell response in a human
30 patient, comprising administering a pharmaceutical composition described herein. The patient may be afflicted with pancreatic cancer, in which case the methods provide

treatment for the disease, or patient considered at risk for such a disease may be treated prophylactically.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a 5 patient a pharmaceutical composition as recited above. The patient may be afflicted with pancreatic cancer, in which case the methods provide treatment for the disease, or patient considered at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological 10 sample with T cells that specifically react with a polypeptide of the present invention, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological 15 sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a polypeptide of the present invention, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that 20 expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a 25 patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of polypeptide disclosed herein; (ii) a 30 polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount

of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for
5 determining the presence or absence of a cancer, preferably a pancreatic cancer, in a patient comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the
10 presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of:
15 (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the
20 patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample, e.g., tumor sample, serum sample, etc., obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a
25 polypeptide of the present invention; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via
30 polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a

complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

- 5 In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a polypeptide of the present invention; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b)
- 10 10 using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

15 Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE SEQUENCE IDENTIFIERS

- SEQ ID NO:1 is the determined cDNA sequence of clone PANC1-R1,
ID NO. 68811.
- 25 SEQ ID NO:2 is the determined cDNA sequence of clone PANC1-R2,
ID NO. 68812.
- SEQ ID NO:3 is the determined cDNA sequence of clone PANC1-R3,
ID NO. 68813.
- 30 SEQ ID NO:4 is the determined cDNA sequence of clone PANC1-R4,
ID NO. 68814.

SEQ ID NO:5 is the determined cDNA sequence of clone PANC1-R5, ID NO. 68815.

SEQ ID NO:6 is the determined cDNA sequence of clone PANC1-R6, ID NO. 68816.

5 SEQ ID NO:7 is the determined cDNA sequence of clone PANC1-R8, ID NO. 68818.

SEQ ID NO:8 is the determined cDNA sequence of clone PANC1-R10, ID NO. 68820.

10 SEQ ID NO:9 is the determined cDNA sequence of clone PANC1-R11, ID NO. 68821.

SEQ ID NO:10 is the determined cDNA sequence of clone PANC1-R12, ID NO. 68822.

15 SEQ ID NO:11 is the determined cDNA sequence of clone PANC1-R13, ID NO. 68823.

SEQ ID NO:12 is the determined cDNA sequence of clone PANC1-R14, ID NO. 68824.

20 SEQ ID NO:13 is the determined cDNA sequence of clone PANC1-R15, ID NO. 68825.

SEQ ID NO:14 is the determined cDNA sequence of clone PANC1-R16, ID NO. 68826.

SEQ ID NO:15 is the determined cDNA sequence of clone PANC1-R17, ID NO. 68827.

25 SEQ ID NO:16 is the determined cDNA sequence of clone PANC1-R18, ID NO. 68828.

SEQ ID NO:17 is the determined cDNA sequence of clone PANC1-R19, ID NO. 68829.

SEQ ID NO:18 is the determined cDNA sequence of clone PANC1-R20, ID NO. 68830.

30 SEQ ID NO:19 is the determined cDNA sequence of clone PANC1-R21, ID NO. 68917.

SEQ ID NO:20 is the determined cDNA sequence of clone PANC1-R22,
ID NO. 68918.

SEQ ID NO:21 is the determined cDNA sequence of clone PANC1-R23,
ID NO. 68919.

5 SEQ ID NO:22 is the determined cDNA sequence of clone PANC1-R24,
ID NO. 68920.

SEQ ID NO:23 is the determined cDNA sequence of clone PANC1-R25,
ID NO. 68921.

10 SEQ ID NO:24 is the determined cDNA sequence of clone PANC1-R27,
ID NO. 68923.

SEQ ID NO:25 is the determined cDNA sequence of clone PANC1-R28,
ID NO. 68924.

SEQ ID NO:26 is the determined cDNA sequence of clone PANC1-R29,
ID NO. 68925.

15 SEQ ID NO:27 is the determined cDNA sequence of clone PANC1-R30,
ID NO. 68926.

SEQ ID NO:28 is the determined cDNA sequence of clone PANC1-R32,
ID NO. 68928.

20 SEQ ID NO:29 is the determined cDNA sequence of clone PANC1-R33,
ID NO. 68929.

SEQ ID NO:30 is the determined cDNA sequence of clone PANC1-R34,
ID NO. 68930.

SEQ ID NO:31 is the determined cDNA sequence of clone PANC1-R36,
ID NO. 68932.

25 SEQ ID NO:32 is the determined cDNA sequence of clone PANC1-R37,
ID NO. 68933.

SEQ ID NO:33 is the determined cDNA sequence of clone PANC1-R39,
ID NO. 68935.

30 SEQ ID NO:34 is the determined cDNA sequence of clone PANC1-R40,
ID NO. 68936.

SEQ ID NO:35 is the determined cDNA sequence of clone PANC1-R43, ID NO. 69117.

SEQ ID NO:36 is the determined cDNA sequence of clone PANC1-R44, ID NO. 69118.

5 SEQ ID NO:37 is the determined cDNA sequence of clone PANC1-R45, ID NO. 69119.

SEQ ID NO:38 is the determined cDNA sequence of clone PANC1-R46, ID NO. 69120.

10 SEQ ID NO:39 is the determined cDNA sequence of clone PANC1-R47, ID NO. 69126.

SEQ ID NO:40 is the determined cDNA sequence of clone PANC1-R50, ID NO. 69133.

SEQ ID NO:41 is the determined cDNA sequence of clone PANC1-R51, ID NO. 69134.

15 SEQ ID NO:42 is the determined cDNA sequence of clone PANC1-R52, ID NO. 69135.

SEQ ID NO:43 is the determined cDNA sequence of clone PANC1-R53, ID NO. 69136.

20 SEQ ID NO:44 is the determined cDNA sequence of clone PANC1-R56, ID NO. 69139.

SEQ ID NO:45 is the determined cDNA sequence of clone PANC1-R59, ID NO. 69142.

SEQ ID NO:46 is the determined cDNA sequence of clone PANC1-R64, ID NO. 69292.

25 SEQ ID NO:47 is the determined cDNA sequence of clone PANC1-R66, ID NO. 69294.

SEQ ID NO:48 is the determined cDNA sequence of clone PANC1-R67, ID NO. 69295.

30 SEQ ID NO:49 is the determined cDNA sequence of clone PANC1-R69, ID NO. 69297.

SEQ ID NO:50 is the determined cDNA sequence of clone PANC1-R70, ID NO. 69298.

SEQ ID NO:51 is the determined cDNA sequence of clone PANC1-R71, ID NO. 69299.

5 SEQ ID NO:52 is the determined cDNA sequence of clone PANC1-R73, ID NO. 69301.

SEQ ID NO:53 is the determined cDNA sequence of clone PANC1-R76 A, ID NO. 69304.

10 SEQ ID NO:54 is the determined cDNA sequence of clone PANC1-R76 B, ID NO. 69304.

SEQ ID NO:55 is the determined cDNA sequence of clone PANC1-R78, ID NO. 69306.

SEQ ID NO:56 is the determined cDNA sequence of clone PANC1-R80, ID NO. 69308.

15 SEQ ID NO:57 is the determined cDNA sequence of clone PANC1-R82, ID NO. 69310.

SEQ ID NO:58 is the determined cDNA sequence of clone PANC1-R83, ID NO. 69311.

20 SEQ ID NO:59 is the determined cDNA sequence of clone PANC1-R84, ID NO. 69312.

SEQ ID NO:60 is the determined cDNA sequence of clone PANC1-R85, ID NO. 69313.

SEQ ID NO:61 is the determined cDNA sequence of clone PANC1-R86, ID NO. 69314.

25 SEQ ID NO:62 is the determined cDNA sequence of clone PANC1-R88, ID NO. 69316.

SEQ ID NO:63 is the determined cDNA sequence of clone PANC1-R89, ID NO. 69317.

30 SEQ ID NO:64 is the determined cDNA sequence of clone PANC1-R90, ID NO. 69318.

SEQ ID NO:65 is the determined cDNA sequence of clone PANC1-R91, ID NO. 69319.

SEQ ID NO:66 is the determined cDNA sequence of clone PANC1-R94, ID NO. 69322.

5 SEQ ID NO:67 is the predicted polypeptide sequence of clone PANC1-R44, ID NO. 69118.

SEQ ID NO:68 is the predicted polypeptide sequence of clone PANC1-R47, ID NO. 69126.

10 SEQ ID NO:69 is the predicted polypeptide sequence of clone PANC1-R64, ID NO. 69292.

SEQ ID NO:70 is the predicted polypeptide sequence of clone PANC1-R66, ID NO. 69294.

SEQ ID NO:71 is the predicted polypeptide sequence of clone PANC1-R76 A, ID NO. 69304.

15 SEQ ID NO:72 is the predicted polypeptide sequence of clone PANC1-R76 B, ID NO. 69304.

SEQ ID NO:73 is the predicted polypeptide sequence of clone PANC1-R85, ID NO. 69313.

20 SEQ ID NO:74 is the predicted polypeptide sequence of clone PANC1-R94, ID NO. 69322.

SEQ ID NO:75 is the determined cDNA sequence of clone 80150.1

SEQ ID NO:76 is the determined cDNA sequence of clone 80151.1

SEQ ID NO:77 is the determined cDNA sequence of clone 80152.1

SEQ ID NO:78 is the determined cDNA sequence of clone 80153.1

25 SEQ ID NO:79 is the determined cDNA sequence of clone 80154.1

SEQ ID NO:80 is the determined cDNA sequence of clone 80155.1

SEQ ID NO:81 is the determined cDNA sequence of clone 80156.1

SEQ ID NO:82 is the determined cDNA sequence of clone 80157.1

SEQ ID NO:83 is the determined cDNA sequence of clone 80158.1

30 SEQ ID NO:84 is the determined cDNA sequence of clone 80159.1

SEQ ID NO:85 is the determined cDNA sequence of clone 80161.1

SEQ ID NO:86 is the determined cDNA sequence of clone 80162.1
SEQ ID NO:87 is the determined cDNA sequence of clone 80163.1
SEQ ID NO:88 is the determined cDNA sequence of clone 80164.1
SEQ ID NO:89 is the determined cDNA sequence of clone 80165.1
5 SEQ ID NO:90 is the determined cDNA sequence of clone 80166.1
SEQ ID NO:91 is the determined cDNA sequence of clone 80167.1
SEQ ID NO:92 is the determined cDNA sequence of clone 80168.1
SEQ ID NO:93 is the determined cDNA sequence of clone 80169.1
SEQ ID NO:94 is the determined cDNA sequence of clone 80170.1
10 SEQ ID NO:95 is the determined cDNA sequence of clone 80171.1
SEQ ID NO:96 is the determined cDNA sequence of clone 80173.1
SEQ ID NO:97 is the determined cDNA sequence of clone 80175.1
SEQ ID NO:98 is the determined cDNA sequence of clone 80176.1
SEQ ID NO:99 is the determined cDNA sequence of clone 80178.1
15 SEQ ID NO:100 is the determined cDNA sequence of clone 80180.1
SEQ ID NO:101 is the determined cDNA sequence of clone 80181.1
SEQ ID NO:102 is the determined cDNA sequence of clone 80183.1
SEQ ID NO:103 is the determined cDNA sequence of clone 80184.1
SEQ ID NO:104 is the determined cDNA sequence of clone 80185.1
20 SEQ ID NO:105 is the determined cDNA sequence of clone 80186.1
SEQ ID NO:106 is the determined cDNA sequence of clone 80187.1
SEQ ID NO:107 is the determined cDNA sequence of clone 80188.1
SEQ ID NO:108 is the determined cDNA sequence of clone 80189.1
SEQ ID NO:109 is the determined cDNA sequence of clone 80191.1
25 SEQ ID NO:110 is the determined cDNA sequence of clone 80192.1
SEQ ID NO:111 is the determined cDNA sequence of clone 80193.1
SEQ ID NO:112 is the determined cDNA sequence of clone 80194.1
SEQ ID NO:113 is the determined cDNA sequence of clone 80195.1
SEQ ID NO:114 is the determined cDNA sequence of clone 80196.1
30 SEQ ID NO:115 is the determined cDNA sequence of clone 80197.1
SEQ ID NO:116 is the determined cDNA sequence of clone 80198.1

SEQ ID NO:117 is the determined cDNA sequence of clone 80199.1
SEQ ID NO:118 is the determined cDNA sequence of clone 80172.2
SEQ ID NO:119 is the determined cDNA sequence of clone 80174.2
SEQ ID NO:120 is the determined cDNA sequence of clone 80177.2
5 SEQ ID NO:121 is the determined cDNA sequence of clone 80179.2
SEQ ID NO:122 is the determined cDNA sequence of clone 80190.2
SEQ ID NO:123 is the determined cDNA sequence of clone 80200.2
SEQ ID NO:124 is the determined cDNA sequence of clone 80201.2
SEQ ID NO:125 is the determined cDNA sequence of clone 80203.2
10 SEQ ID NO:126 is the determined cDNA sequence of clone 80204.2
SEQ ID NO:127 is the determined cDNA sequence of clone 80205.2
SEQ ID NO:128 is the determined cDNA sequence of clone 80207.2
SEQ ID NO:129 is the determined cDNA sequence of clone 80208.2
SEQ ID NO:130 is the full-length determined cDNA sequence of clone
15 PIGPC1
SEQ ID NO:131 is the full-length determined cDNA sequence of clone
SERPINE1
SEQ ID NO:132 is the full-length determined cDNA sequence of clone
KRT18
20 RABGGTB
SEQ ID NO:133 is the full-length determined cDNA sequence of clone
hFAT
SEQ ID NO:134 is the full-length determined cDNA sequence of clone
25 FBL
SEQ ID NO:135 is the full-length determined cDNA sequence of clone
COL1al
SEQ ID NO:136 is the full-length determined cDNA sequence of clone
pM5
SEQ ID NO:137 is the full-length determined cDNA sequence of clone
30 PSK-1
SEQ ID NO:138 is the full-length determined cDNA sequence of clone

SEQ ID NO:139 is the full-length determined cDNA sequence of clone
CD24

SEQ ID NO:140 is the determined cDNA sequence of clone
sim.toHu.G6PD

5 SEQ ID NO:141 is the full-length determined cDNA sequence of clone
GdX

SEQ ID NO:142 is the full-length determined cDNA sequence of clone
PLS3

SEQ ID NO:143 is the full-length determined cDNA sequence of clone
10 LISCH7

SEQ ID NO:144 is the full-length determined cDNA sequence of clone
COL18A1

SEQ ID NO:145 is the full-length determined cDNA sequence of clone
TFPI2

15 SEQ ID NO:146 is the full-length determined cDNA sequence of clone
L6

SEQ ID NO:147 is the full-length determined cDNA sequence of clone
SERF1A

SEQ ID NO:148 is the full-length determined cDNA sequence of clone
20 SERF1B

SEQ ID NO:149 is the full-length determined cDNA sequence of clone
THBS2

SEQ ID NO:150 is the full-length determined cDNA sequence of clone
SEMA3C

25 SEQ ID NO:151 is the full-length determined cDNA sequence of clone
CTGF

SEQ ID NO:152 is the full-length determined cDNA sequence of clone
pHL-1

SEQ ID NO:153 is the full-length predicted amino acid sequence of
30 clone PICPC1

SEQ ID NO:154 is the full-length predicted amino acid sequence of clone SERPINE1

SEQ ID NO:155 is the full-length predicted amino acid sequence of clone KRT18

5 SEQ ID NO:156 is the full-length predicted amino acid sequence of clone RABGGTB

SEQ ID NO:157 is the full-length predicted amino acid sequence of clone hFAT

10 SEQ ID NO:158 is the full-length predicted amino acid sequence of clone FBL

SEQ ID NO:159 is the full-length predicted amino acid sequence of clone COL1a1

15 SEQ ID NO:160 is the full-length predicted amino acid sequence of clone pM5

clone PSK-1

SEQ ID NO:162 is the full-length predicted amino acid sequence of clone CD24

20 SEQ ID NO:163 is the full-length predicted amino acid sequence of clone GdX

SEQ ID NO:164 is the full-length predicted amino acid sequence of clone PLS3

SEQ ID NO:165 is the full-length predicted amino acid sequence of clone LISCH7

25 SEQ ID NO:166 is the full-length predicted amino acid sequence of clone COL18A1

SEQ ID NO:167 is the full-length predicted amino acid sequence of clone TFPI2

30 SEQ ID NO:168 is the full-length predicted amino acid sequence of clone L6

SEQ ID NO:169 is the full-length predicted amino acid sequence of clone SERF1A.

SEQ ID NO:170 is the full-length predicted amino acid sequence of clone SERF1B.

5 SEQ ID NO:171 is the full-length predicted amino acid sequence of clone THBS2.

SEQ ID NO:172 is the full-length predicted amino acid sequence of clone SEMA3C.

10 SEQ ID NO:173 is the full-length predicted amino acid sequence of clone CTGF.

SEQ ID NO:174 is the full-length determined cDNA sequence of clone HECH.

SEQ ID NO:175 is the full-length determined cDNA sequence of clone SCD.

15 SEQ ID NO:176 is the full-length determined cDNA sequence of clone CHGB.

SEQ ID NO:177 is the full-length determined cDNA sequence of clone FER1L3.

20 SEQ ID NO:178 is the full-length predicted amino acid sequence of clone HECH.

SEQ ID NO:179 is the full-length predicted amino acid sequence of clone SCD.

SEQ ID NO:180 is the full-length predicted amino acid sequence of clone CHGB.

25 SEQ ID NO:181 is the full-length predicted amino acid sequence of clone FER1L3.

SEQ ID NO:182 is the full-length determined cDNA sequence of clone MGC15409.

SEQ ID NO:183 is the full-length predicted amino acid sequence of clone MGC15409.

30 SEQ ID NO:184 is the determined cDNA sequence of clone 71231.1.

SEQ ID NO:185 is the determined cDNA sequence of clone 71232.1
SEQ ID NO:186 is the determined cDNA sequence of clone 71233.1
SEQ ID NO:187 is the determined cDNA sequence of clone 71234.1
SEQ ID NO:188 is the determined cDNA sequence of clone 71235.1
5 SEQ ID NO:189 is the determined cDNA sequence of clone 71236.1
SEQ ID NO:190 is the determined cDNA sequence of clone 71237.1
SEQ ID NO:191 is the determined cDNA sequence of clone 73408.1
SEQ ID NO:192 is the determined cDNA sequence of clone 73409.1
SEQ ID NO:193 is the determined cDNA sequence of clone 73410.1
10 SEQ ID NO:194 is the determined cDNA sequence of clone 71238.1
SEQ ID NO:195 is the determined cDNA sequence of clone 73411.1
SEQ ID NO:196 is the determined cDNA sequence of clone 71239.1
SEQ ID NO:197 is the determined cDNA sequence of clone 73412.3
SEQ ID NO:198 is the determined cDNA sequence of clone 73412.2
15 SEQ ID NO:199 is the determined cDNA sequence of clone 71240.1
SEQ ID NO:200 is the determined cDNA sequence of clone 71241.1
SEQ ID NO:201 is the determined cDNA sequence of clone 71242.1
SEQ ID NO:202 is the determined cDNA sequence of clone 73413.2
SEQ ID NO:203 is the determined cDNA sequence of clone 71243.1
20 SEQ ID NO:204 is the determined cDNA sequence of clone 71244.1
SEQ ID NO:205 is the determined cDNA sequence of clone 71245.1
SEQ ID NO:206 is the determined cDNA sequence of clone 71246.1
SEQ ID NO:207 is the determined cDNA sequence of clone 71247.1
SEQ ID NO:208 is the determined cDNA sequence of clone 71248.1
25 SEQ ID NO:209 is the determined cDNA sequence of clone 71249.1
SEQ ID NO:210 is the determined cDNA sequence of clone 73414.2
SEQ ID NO:211 is the determined cDNA sequence of clone 71250.1
SEQ ID NO:212 is the determined cDNA sequence of clone 71251.1
SEQ ID NO:213 is the determined cDNA sequence of clone 71252.1
30 SEQ ID NO:214 is the determined cDNA sequence of clone 71253.1
SEQ ID NO:215 is the determined cDNA sequence of clone 71254.3

SEQ ID NO:216 is the determined cDNA sequence of clone 71255.2
SEQ ID NO:217 is the determined cDNA sequence of clone 71255.3
SEQ ID NO:218 is the determined cDNA sequence of clone 71256.1
SEQ ID NO:219 is the determined cDNA sequence of clone 73415.1
5 SEQ ID NO:220 is the determined cDNA sequence of clone 71257.1
SEQ ID NO:221 is the determined cDNA sequence of clone 71258.1
SEQ ID NO:222 is the determined cDNA sequence of clone 71259.1
SEQ ID NO:223 is the determined cDNA sequence of clone 73416.1
SEQ ID NO:224 is the determined cDNA sequence of clone 71260.1
10 SEQ ID NO:225 is the determined cDNA sequence of clone 73376.1
SEQ ID NO:226 is the determined cDNA sequence of clone 73377.1
SEQ ID NO:227 is the determined cDNA sequence of clone 73378.1
SEQ ID NO:228 is the determined cDNA sequence of clone 73379.2
SEQ ID NO:229 is the determined cDNA sequence of clone 73381.3
15 SEQ ID NO:230 is the determined cDNA sequence of clone 73381.2
SEQ ID NO:231 is the determined cDNA sequence of clone 73382.1
SEQ ID NO:232 is the determined cDNA sequence of clone 73383.2
SEQ ID NO:233 is the determined cDNA sequence of clone 73383.3
SEQ ID NO:234 is the determined cDNA sequence of clone 73384.2
20 SEQ ID NO:235 is the determined cDNA sequence of clone 73384.3
SEQ ID NO:236 is the determined cDNA sequence of clone 73385.1
SEQ ID NO:237 is the determined cDNA sequence of clone 73386.1
SEQ ID NO:238 is the determined cDNA sequence of clone 73387.1
SEQ ID NO:239 is the determined cDNA sequence of clone 73388.2
25 SEQ ID NO:240 is the determined cDNA sequence of clone 73388.3
SEQ ID NO:241 is the determined cDNA sequence of clone 73389.2
SEQ ID NO:242 is the determined cDNA sequence of clone 73389.3
SEQ ID NO:243 is the determined cDNA sequence of clone 73390.1
SEQ ID NO:244 is the determined cDNA sequence of clone 73391.2
30 SEQ ID NO:245 is the determined cDNA sequence of clone 73417.2
SEQ ID NO:246 is the determined cDNA sequence of clone 73392.1

SEQ ID NO:247 is the determined cDNA sequence of clone 73393.3
SEQ ID NO:248 is the determined cDNA sequence of clone 73418.1
SEQ ID NO:249 is the determined cDNA sequence of clone 73395.1
SEQ ID NO:250 is the determined cDNA sequence of clone 73396.1
5 SEQ ID NO:251 is the determined cDNA sequence of clone 73397.1
SEQ ID NO:252 is the determined cDNA sequence of clone 73419.3
SEQ ID NO:253 is the determined cDNA sequence of clone 73419.2
SEQ ID NO:254 is the determined cDNA sequence of clone 73398.1
SEQ ID NO:255 is the determined cDNA sequence of clone 73399.3
10 SEQ ID NO:256 is the determined cDNA sequence of clone 73399.2
SEQ ID NO:257 is the determined cDNA sequence of clone 73400.1
SEQ ID NO:258 is the determined cDNA sequence of clone 73420.3
SEQ ID NO:259 is the determined cDNA sequence of clone 73420.2
SEQ ID NO:260 is the determined cDNA sequence of clone 73401.1
15 SEQ ID NO:261 is the determined cDNA sequence of clone 73404.3
SEQ ID NO:262 is the determined cDNA sequence of clone 73405.1
SEQ ID NO:263 is the determined cDNA sequence of clone 73407.3
SEQ ID NO:264 is the determined cDNA sequence of clone 73407.2
SEQ ID NO:265 is the determined cDNA sequence of clone 72174.1
20 SEQ ID NO:266 is the determined cDNA sequence of clone 72175.1
SEQ ID NO:267 is the determined cDNA sequence of clone 72176.1
SEQ ID NO:268 is the determined cDNA sequence of clone 72177.1
SEQ ID NO:269 is the determined cDNA sequence of clone 72178.1
SEQ ID NO:270 is the determined cDNA sequence of clone 72179.1
25 SEQ ID NO:271 is the determined cDNA sequence of clone 73421.3
SEQ ID NO:272 is the determined cDNA sequence of clone 73421.2
SEQ ID NO:273 is the determined cDNA sequence of clone 72180.1
SEQ ID NO:274 is the determined cDNA sequence of clone 72181.1
SEQ ID NO:275 is the determined cDNA sequence of clone 72182.1
30 SEQ ID NO:276 is the determined cDNA sequence of clone 72183.1
SEQ ID NO:277 is the determined cDNA sequence of clone 72184.1

SEQ ID NO:278 is the determined cDNA sequence of clone 72185.1
SEQ ID NO:279 is the determined cDNA sequence of clone 72186.1
SEQ ID NO:280 is the determined cDNA sequence of clone 72187.1
SEQ ID NO:281 is the determined cDNA sequence of clone 72188.1
5 SEQ ID NO:282 is the determined cDNA sequence of clone 72189.1
SEQ ID NO:283 is the determined cDNA sequence of clone 72190.1
SEQ ID NO:284 is the determined cDNA sequence of clone 72191.1
SEQ ID NO:285 is the determined cDNA sequence of clone 72192.1
SEQ ID NO:286 is the determined cDNA sequence of clone 72193.1
10 SEQ ID NO:287 is the determined cDNA sequence of clone 72194.1
SEQ ID NO:288 is the determined cDNA sequence of clone 72195.1
SEQ ID NO:289 is the determined cDNA sequence of clone 72196.1
SEQ ID NO:290 is the determined cDNA sequence of clone 72197.1
SEQ ID NO:291 is the determined cDNA sequence of clone 72198.1
15 SEQ ID NO:292 is the determined cDNA sequence of clone 72199.1
SEQ ID NO:293 is the determined cDNA sequence of clone 72200.1
SEQ ID NO:294 is the determined cDNA sequence of clone 72201.1
SEQ ID NO:295 is the determined cDNA sequence of clone 72202.1
SEQ ID NO:296 is the determined cDNA sequence of clone 72203.1
20 SEQ ID NO:297 is the determined cDNA sequence of clone 72204.1
SEQ ID NO:298 is the determined cDNA sequence of clone 72205.1
SEQ ID NO:299 is the determined cDNA sequence of clone 72206.3
SEQ ID NO:300 is the determined cDNA sequence of clone 72206.2
SEQ ID NO:301 is the determined cDNA sequence of clone 73422.1
25 SEQ ID NO:302 is the determined cDNA sequence of clone 73423.1
SEQ ID NO:303 is the determined cDNA sequence of clone 73424.1
SEQ ID NO:304 is the determined cDNA sequence of clone 73425.3
SEQ ID NO:305 is the determined cDNA sequence of clone 73425.2
SEQ ID NO:306 is the determined cDNA sequence of clone 74597.2
30 SEQ ID NO:307 is the determined cDNA sequence of clone 73426.3
SEQ ID NO:308 is the determined cDNA sequence of clone 73426.2

SEQ ID NO:309 is the determined cDNA sequence of clone 73427.3
SEQ ID NO:310 is the determined cDNA sequence of clone 73427.2
SEQ ID NO:311 is the determined cDNA sequence of clone 73428.3
SEQ ID NO:312 is the determined cDNA sequence of clone 73429.3
5 SEQ ID NO:313 is the determined cDNA sequence of clone 74598.1
SEQ ID NO:314 is the determined cDNA sequence of clone 74598.2
SEQ ID NO:315 is the determined cDNA sequence of clone 74599.2
SEQ ID NO:316 is the determined cDNA sequence of clone 73430.3
SEQ ID NO:317 is the determined cDNA sequence of clone 74600.1
10 SEQ ID NO:318 is the determined cDNA sequence of clone 74600.2
SEQ ID NO:319 is the determined cDNA sequence of clone 74601.1
SEQ ID NO:320 is the determined cDNA sequence of clone 74602.2
SEQ ID NO:321 is the determined cDNA sequence of clone 73437.2
SEQ ID NO:322 is the determined cDNA sequence of clone 73437.3
15 SEQ ID NO:323 is the determined cDNA sequence of clone 73438.2
SEQ ID NO:324 is the determined cDNA sequence of clone 73438.3
SEQ ID NO:325 is the determined cDNA sequence of clone 73439.2
SEQ ID NO:326 is the determined cDNA sequence of clone 73439.3
SEQ ID NO:327 is the determined cDNA sequence of clone 73440.2
20 SEQ ID NO:328 is the determined cDNA sequence of clone 73440.3
SEQ ID NO:329 is the determined cDNA sequence of clone 73441.3
SEQ ID NO:330 is the determined cDNA sequence of clone 73442.2
SEQ ID NO:331 is the determined cDNA sequence of clone 73442.3
SEQ ID NO:332 is the determined cDNA sequence of clone 73443.2
25 SEQ ID NO:333 is the determined cDNA sequence of clone 73443.3
SEQ ID NO:334 is the determined cDNA sequence of clone 73444.2
SEQ ID NO:335 is the determined cDNA sequence of clone 73444.3
SEQ ID NO:336 is the determined cDNA sequence of clone 74602.1
SEQ ID NO:337 is the determined cDNA sequence of clone 73445.1
30 SEQ ID NO:338 is the determined cDNA sequence of clone 73456.1
SEQ ID NO:339 is the determined cDNA sequence of clone 73585.3

SEQ ID NO:340 is the determined cDNA sequence of clone 73586.2
SEQ ID NO:341 is the determined cDNA sequence of clone 73586.3
SEQ ID NO:342 is the determined cDNA sequence of clone 73587.2
SEQ ID NO:343 is the determined cDNA sequence of clone 73587.3
5 SEQ ID NO:344 is the determined cDNA sequence of clone 73457.2
SEQ ID NO:345 is the determined cDNA sequence of clone 73457.3
SEQ ID NO:346 is the determined cDNA sequence of clone 74603.1
SEQ ID NO:347 is the determined cDNA sequence of clone 74603.2
SEQ ID NO:348 is the determined cDNA sequence of clone 73458.1
10 SEQ ID NO:349 is the determined cDNA sequence of clone 73459.2
SEQ ID NO:350 is the determined cDNA sequence of clone 73459.3
SEQ ID NO:351 is the determined cDNA sequence of clone 73460.2
SEQ ID NO:352 is the determined cDNA sequence of clone 73460.3
SEQ ID NO:353 is the determined cDNA sequence of clone 73461.1
15 SEQ ID NO:354 is the determined cDNA sequence of clone 74604.1
SEQ ID NO:355 is the determined cDNA sequence of clone 74604.2
SEQ ID NO:356 is the determined cDNA sequence of clone 74605.1
SEQ ID NO:357 is the determined cDNA sequence of clone 74605.2
SEQ ID NO:358 is the determined cDNA sequence of clone 74606.1
20 SEQ ID NO:359 is the determined cDNA sequence of clone 74606.2
SEQ ID NO:360 is the determined cDNA sequence of clone 74607.1
SEQ ID NO:361 is the determined cDNA sequence of clone 74607.2
SEQ ID NO:362 is the determined cDNA sequence of clone 74608.1
SEQ ID NO:363 is the determined cDNA sequence of clone 74608.2
25 SEQ ID NO:364 is the determined cDNA sequence of clone 74610.2
SEQ ID NO:365 is the determined cDNA sequence of clone 74611.1
SEQ ID NO:366 is the determined cDNA sequence of clone 74613.1
SEQ ID NO:367 is the determined cDNA sequence of clone 74613.2
SEQ ID NO:368 is the determined cDNA sequence of clone 74614.1
30 SEQ ID NO:369 is the determined cDNA sequence of clone 74614.2
SEQ ID NO:370 is the determined cDNA sequence of clone 74640.2

SEQ ID NO:371 is the determined cDNA sequence of clone 74640.1
SEQ ID NO:372 is the determined cDNA sequence of clone 74615.2
SEQ ID NO:373 is the determined cDNA sequence of clone 74615.1
SEQ ID NO:374 is the determined cDNA sequence of clone 74616.2
5 SEQ ID NO:375 is the determined cDNA sequence of clone 74616.1
SEQ ID NO:376 is the determined cDNA sequence of clone 74617.2
SEQ ID NO:377 is the determined cDNA sequence of clone 77101.1
SEQ ID NO:378 is the determined cDNA sequence of clone 77102.1
SEQ ID NO:379 is the determined cDNA sequence of clone 77104.1
10 SEQ ID NO:380 is the determined cDNA sequence of clone 74618.1
SEQ ID NO:381 is the determined cDNA sequence of clone 74618.2
SEQ ID NO:382 is the determined cDNA sequence of clone 74619.2
SEQ ID NO:383 is the determined cDNA sequence of clone 74620.1
SEQ ID NO:384 is the determined cDNA sequence of clone 74620.2
15 SEQ ID NO:385 is the determined cDNA sequence of clone 74621.1
SEQ ID NO:386 is the determined cDNA sequence of clone 74621.2
SEQ ID NO:387 is the determined cDNA sequence of clone 74623.1
SEQ ID NO:388 is the determined cDNA sequence of clone 74623.2
SEQ ID NO:389 is the determined cDNA sequence of clone 74624.1
20 SEQ ID NO:390 is the determined cDNA sequence of clone 74624.2
SEQ ID NO:391 is the determined cDNA sequence of clone 74625.1
SEQ ID NO:392 is the determined cDNA sequence of clone 74625.2
SEQ ID NO:393 is the determined cDNA sequence of clone 74631.2
SEQ ID NO:394 is the determined cDNA sequence of clone 74632.1
25 SEQ ID NO:395 is the determined cDNA sequence of clone 74632.2
SEQ ID NO:396 is the determined cDNA sequence of clone 77105.1
SEQ ID NO:397 is the determined cDNA sequence of clone 77108.1
SEQ ID NO:398 is the determined cDNA sequence of clone 77109.1
SEQ ID NO:399 is the determined cDNA sequence of clone 77114.1
30 SEQ ID NO:400 is the determined cDNA sequence of clone 77118.1
SEQ ID NO:401 is the determined cDNA sequence of clone 77120.1

SEQ ID NO:402 is the determined cDNA sequence of clone 77122.1
SEQ ID NO:403 is the determined cDNA sequence of clone 77123.1
SEQ ID NO:404 is the determined cDNA sequence of clone 77125.1
SEQ ID NO:405 is the determined cDNA sequence of clone 77127.1
5 SEQ ID NO:406 is the determined cDNA sequence of clone 77129.1
SEQ ID NO:407 is the determined cDNA sequence of clone 77130.1
SEQ ID NO:408 is the determined cDNA sequence of clone 77132.1
SEQ ID NO:409 is the determined cDNA sequence of clone 77134.1
SEQ ID NO:410 is the determined cDNA sequence of clone 77135.1
10 SEQ ID NO:411 is the determined cDNA sequence of clone 77136.1
SEQ ID NO:412 is the determined cDNA sequence of clone 77139.1
SEQ ID NO:413 is the determined cDNA sequence of clone 77140.1
SEQ ID NO:414 is the determined cDNA sequence of clone 77141.1
SEQ ID NO:415 is the determined cDNA sequence of clone 77144.1
15 SEQ ID NO:416 is the determined cDNA sequence of clone 77146.1
SEQ ID NO:417 is the determined cDNA sequence of clone 77149.1
SEQ ID NO:418 is the determined cDNA sequence of clone 77474.1
SEQ ID NO:419 is the determined cDNA sequence of clone 77153.1
SEQ ID NO:420 is the determined cDNA sequence of clone 77479.1
20 SEQ ID NO:421 is the determined cDNA sequence of clone 77154.1
SEQ ID NO:422 is the determined cDNA sequence of clone 77155.1
SEQ ID NO:423 is the determined cDNA sequence of clone 77157.1
SEQ ID NO:424 is the determined cDNA sequence of clone 77480.1
SEQ ID NO:425 is the determined cDNA sequence of clone 77485.1
25 SEQ ID NO:426 is the determined cDNA sequence of clone 77487.1
SEQ ID NO:427 is the determined cDNA sequence of clone 77488.1
SEQ ID NO:428 is the determined cDNA sequence of clone 77490.1
SEQ ID NO:429 is the determined cDNA sequence of clone 77494.1
SEQ ID NO:430 is the determined cDNA sequence of clone 77495.1
30 SEQ ID NO:431 is the determined cDNA sequence of clone 77499.1
SEQ ID NO:432 is the determined cDNA sequence of clone 77500.1

SEQ ID NO:433 is the determined cDNA sequence of clone 77160.1
SEQ ID NO:434 is the determined cDNA sequence of clone 77504.1
SEQ ID NO:435 is the determined cDNA sequence of clone 77506.1
SEQ ID NO:436 is the determined cDNA sequence of clone 77507.1
5 SEQ ID NO:437 is the determined cDNA sequence of clone 77508.1
SEQ ID NO:438 is the determined cDNA sequence of clone 77509.1
SEQ ID NO:439 is the determined cDNA sequence of clone 77162.1
SEQ ID NO:440 is the determined cDNA sequence of clone 77163.1
SEQ ID NO:441 is the determined cDNA sequence of clone 77165.1
10 SEQ ID NO:442 is the determined cDNA sequence of clone 77167.1
SEQ ID NO:443 is the determined cDNA sequence of clone 77169.1
SEQ ID NO:444 is the determined cDNA sequence of clone 77171.1
SEQ ID NO:445 is the determined cDNA sequence of clone 77172.1
SEQ ID NO:446 is the determined cDNA sequence of clone 77173.1
15 SEQ ID NO:447 is the determined cDNA sequence of clone 77175.1
SEQ ID NO:448 is the determined cDNA sequence of clone 77176.1
SEQ ID NO:449 is the determined cDNA sequence of clone 77178.1
SEQ ID NO:450 is the determined cDNA sequence of clone 77180.1
SEQ ID NO:451 is the determined cDNA sequence of clone 77510.1
20 SEQ ID NO:452 is the full-length determined cDNA sequence for coxIII
SEQ ID NO:453 is the full-length predicted amino acid sequence of
coxIII
SEQ ID NO:454 is the determined full-length cDNA sequence of clone
80186 (also referred to as Pn80E), extending the sequence set forth in SEQ ID NO:105
25 SEQ ID NO:455 is the full-length cDNA sequence of Pn81E.
SEQ ID NO:456 is the determined cDNA sequence of clone PaSLBH2c1
SEQ ID NO:457 is the determined cDNA sequence of clone PaSLBH2c2
SEQ ID NO:458 is the determined cDNA sequence of clone PaSLBH2c3
SEQ ID NO:459 is the determined cDNA sequence of clone PaSLBH2c4
30 SEQ ID NO:460 is the determined cDNA sequence of clone PaSLBH2c5
SEQ ID NO:461 is the determined cDNA sequence of clone PaSLBH2c7

SEQ ID NO:462 is the determined cDNA sequence of clone PaSLBH2c8
SEQ ID NO:463 is the determined cDNA sequence of clone PaSLBH2c9
SEQ ID NO:464 is the determined cDNA sequence of clone
PaSLBH2c10

5 SEQ ID NO:465 is the determined cDNA sequence of clone
PaSLBH2c11

 SEQ ID NO:466 is the determined cDNA sequence of clone
PaSLBH2c12

 SEQ ID NO:467 is the determined cDNA sequence of clone
10 PaSLBH2c13

 SEQ ID NO:468 is the determined cDNA sequence of clone
PaSLBH2c14

 SEQ ID NO:469 is the determined cDNA sequence of clone
PaSLBH2c15

15 SEQ ID NO:470 is the determined cDNA sequence of clone
PaSLBH2c16

 SEQ ID NO:471 is the determined cDNA sequence of clone
PaSLBH2c17

 SEQ ID NO:472 is the determined cDNA sequence of clone
20 PaSLBH2c18

 SEQ ID NO:473 is the determined cDNA sequence of clone
PaSLBH2c19

 SEQ ID NO:474 is the determined cDNA sequence of clone
PaSLBH2c20

25 SEQ ID NO:475 is the determined cDNA sequence of clone
PaSLBH2c21

 SEQ ID NO:476 is the determined cDNA sequence of clone
PaSLBH2c22

 SEQ ID NO:477 is the determined cDNA sequence of clone
30 PaSLBH2c23

SEQ ID NO:478 is the determined cDNA sequence of clone
PaSLBH2c24

SEQ ID NO:479 is the determined cDNA sequence of clone
PaSLBH2c25

5 SEQ ID NO:480 is the determined cDNA sequence of clone
PaSLBH2c26

 SEQ ID NO:481 is the determined cDNA sequence of clone
PaSLBH2c27

 SEQ ID NO:482 is the determined cDNA sequence of clone
10 PaSLBH2c28

 SEQ ID NO:483 is the determined cDNA sequence of clone
PaSLBH2c29

 SEQ ID NO:484 is the determined cDNA sequence of clone
PaSLBH2c30

15 SEQ ID NO:485 is the determined cDNA sequence of clone
PaSLBH2c31

 SEQ ID NO:486 is the determined cDNA sequence of clone
PaSLBH2c32

 SEQ ID NO:487 is the determined cDNA sequence of clone
20 PaSLBH2c33

 SEQ ID NO:488 is the determined cDNA sequence of clone
PaSLBH2c34

 SEQ ID NO:489 is the determined cDNA sequence of clone
PaSLBH2c35

25 SEQ ID NO:490 is the determined cDNA sequence of clone
PaSLBH2c36

 SEQ ID NO:491 is the determined cDNA sequence of clone
PaSLBH2c37

 SEQ ID NO:492 is the determined cDNA sequence of clone
30 PaSLBH2c38

SEQ ID NO:493 is the determined cDNA sequence of clone
PaSLBH2c39

SEQ ID NO:494 is the determined cDNA sequence of clone
PASLBH2bc1

5 SEQ ID NO:495 is the determined cDNA sequence of clone
PASLBH2bc2

SEQ ID NO:496 is the determined cDNA sequence of clone
PASLBH2bc3

10 SEQ ID NO:497 is the determined cDNA sequence of clone
PASLBH2bc4

SEQ ID NO:498 is the determined cDNA sequence of clone
PASLBH2bc5

SEQ ID NO:499 is the determined cDNA sequence of clone
PASLBH2bc6

15 SEQ ID NO:500 is the determined cDNA sequence of clone
PASLBH2bc7

SEQ ID NO:501 is the determined cDNA sequence of clone
PASLBH2bc8

20 SEQ ID NO:502 is the determined cDNA sequence of clone
PASLBH2bc10

SEQ ID NO:503 is the determined cDNA sequence of clone
PASLBH2bc11

SEQ ID NO:504 is the determined cDNA sequence of clone
PASLBH2bc12

25 SEQ ID NO:505 is the determined cDNA sequence of clone
PASLBH2bc13

SEQ ID NO:506 is the determined cDNA sequence of clone
PASLBH2bc14

SEQ ID NO:507 is the determined cDNA sequence of clone
30 PASLBH2bc15

SEQ ID NO:508 is the determined cDNA sequence of clone
PASLBH2bc16

SEQ ID NO:509 is the determined cDNA sequence of clone
PASLBH2bc17

5 SEQ ID NO:510 is the determined cDNA sequence of clone
PASLBH2bc18

SEQ ID NO:511 is the determined cDNA sequence of clone
PASLBH2bc19

10 SEQ ID NO:512 is the determined cDNA sequence of clone
PASLBH2bc20

SEQ ID NO:513 is the determined cDNA sequence of clone
PASLBH2bc21

15 SEQ ID NO:514 is the determined cDNA sequence of clone
PASLBH2bc22

SEQ ID NO:515 is the determined cDNA sequence of clone
PASLBH2bc23

20 SEQ ID NO:516 is the determined cDNA sequence of clone
PASLBH2bc24

SEQ ID NO:517 is the determined cDNA sequence of clone
PASLBH2bc25

25 SEQ ID NO:518 is the determined cDNA sequence of clone
PASLBH2bc26

SEQ ID NO:519 is the determined cDNA sequence of clone
PASLBH2bc27

25 SEQ ID NO:520 is the determined cDNA sequence of clone
PASLBH2bc28

SEQ ID NO:521 is the determined cDNA sequence of clone
PASLBH2bc29

30 SEQ ID NO:522 is the determined cDNA sequence of clone
PASLBH2bc30

SEQ ID NO:523 is the determined cDNA sequence of clone
PASLBH2bc31

SEQ ID NO:524 is the determined cDNA sequence of clone
PASLBH2bc32

5 SEQ ID NO:525 is the determined cDNA sequence of clone
PASLBH2bc33

SEQ ID NO:526 is the determined cDNA sequence of clone
PASLBH2bc35

10 SEQ ID NO:527 is the determined cDNA sequence of clone
PASLBH2bc36

SEQ ID NO:528 is the determined cDNA sequence of clone
PASLBH2bc37

15 SEQ ID NO:529 is the determined cDNA sequence of clone 61219685

SEQ ID NO:530 is the determined cDNA sequence of clone 61219686

15 SEQ ID NO:531 is the determined cDNA sequence of clone 61219688

SEQ ID NO:532 is the determined cDNA sequence of clone 61219689

SEQ ID NO:533 is the determined cDNA sequence of clone 61219690

SEQ ID NO:534 is the determined cDNA sequence of clone 61219691

SEQ ID NO:535 is the determined cDNA sequence of clone 61219692

20 SEQ ID NO:536 is the determined cDNA sequence of clone 61219693

SEQ ID NO:537 is the determined cDNA sequence of clone 61219694

SEQ ID NO:538 is the determined cDNA sequence of clone 61219695

SEQ ID NO:539 is the determined cDNA sequence of clone 61219696

SEQ ID NO:540 is the determined cDNA sequence of clone 61219697

25 SEQ ID NO:541 is the determined cDNA sequence of clone 61219698

SEQ ID NO:542 is the determined cDNA sequence of clone 61219699

SEQ ID NO:543 is the determined cDNA sequence of clone 61219700

SEQ ID NO:544 is the determined cDNA sequence of clone 61219701

SEQ ID NO:545 is the determined cDNA sequence of clone 61219704

30 SEQ ID NO:546 is the determined cDNA sequence of clone 61219705

SEQ ID NO:547 is the determined cDNA sequence of clone 61219706

SEQ ID NO:548 is the determined cDNA sequence of clone 61219708
SEQ ID NO:549 is the determined cDNA sequence of clone 61219709
SEQ ID NO:550 is the determined cDNA sequence of clone 61219710
SEQ ID NO:551 is the determined cDNA sequence of clone 61219711
5 SEQ ID NO:552 is the determined cDNA sequence of clone 61219712
SEQ ID NO:553 is the determined cDNA sequence of clone 61219713
SEQ ID NO:554 is the determined cDNA sequence of clone 61219714
SEQ ID NO:555 is the determined cDNA sequence of clone 61219715
SEQ ID NO:556 is the determined cDNA sequence of clone 61219716
10 SEQ ID NO:557 is the determined cDNA sequence of clone 61219717
SEQ ID NO:558 is the determined cDNA sequence of clone 61219718
SEQ ID NO:559 is the determined cDNA sequence of clone 61219720
SEQ ID NO:560 is the determined cDNA sequence of clone 61219721
SEQ ID NO:561 is the determined cDNA sequence of clone 61219723
15 SEQ ID NO:562 is the determined cDNA sequence of clone 61219725
SEQ ID NO:563 is the determined cDNA sequence of clone 61219726
SEQ ID NO:564 is the determined cDNA sequence of clone 61219727
SEQ ID NO:565 is the determined cDNA sequence of clone 61219728
SEQ ID NO:566 is the determined cDNA sequence of clone 61219729
20 SEQ ID NO:567 is the determined cDNA sequence of clone 61219730
SEQ ID NO:568 is the determined cDNA sequence of clone 61219731
SEQ ID NO:569 is the determined cDNA sequence of clone 61219732
SEQ ID NO:570 is the determined cDNA sequence of clone 61219733
SEQ ID NO:571 is the determined cDNA sequence of clone 61219735
25 SEQ ID NO:572 is the determined cDNA sequence of clone 61219736
SEQ ID NO:573 is the determined cDNA sequence of clone 61219738
SEQ ID NO:574 is the determined cDNA sequence of clone 61219739
SEQ ID NO:575 is the determined cDNA sequence of clone 61219740
SEQ ID NO:576 is the determined cDNA sequence of clone 61219741
30 SEQ ID NO:577 is the determined cDNA sequence of clone 61219742
SEQ ID NO:578 is the determined cDNA sequence of clone 61219744

SEQ ID NO:579 is the determined cDNA sequence of clone 61219745
SEQ ID NO:580 is the determined cDNA sequence of clone 61219747
SEQ ID NO:581 is the determined cDNA sequence of clone 61219748
SEQ ID NO:582 is the determined cDNA sequence of clone 61219749
5 SEQ ID NO:583 is the determined cDNA sequence of clone 61219750
SEQ ID NO:584 is the determined cDNA sequence of clone 61219752
SEQ ID NO:585 is the determined cDNA sequence of clone 61219753
SEQ ID NO:586 is the determined cDNA sequence of clone 61219755
SEQ ID NO:587 is the determined cDNA sequence of clone 61219756
10 SEQ ID NO:588 is the determined cDNA sequence of clone 61219757
SEQ ID NO:589 is the determined cDNA sequence of clone 61219759
SEQ ID NO:590 is the determined cDNA sequence of clone 61219761
SEQ ID NO:591 is the determined cDNA sequence of clone 61219762
SEQ ID NO:592 is the determined cDNA sequence of clone 61219763
15 SEQ ID NO:593 is the determined cDNA sequence of clone 61219764
SEQ ID NO:594 is the determined cDNA sequence of clone 61219765
SEQ ID NO:595 is the determined cDNA sequence of clone 61219766
SEQ ID NO:596 is the determined cDNA sequence of clone 61219767
SEQ ID NO:597 is the determined cDNA sequence of clone 61219768
20 SEQ ID NO:598 is the determined cDNA sequence of clone 61219771
SEQ ID NO:599 is the determined cDNA sequence of clone 61219772
SEQ ID NO:600 is the determined cDNA sequence of clone 61219773
SEQ ID NO:601 is the determined cDNA sequence of clone 61219774
SEQ ID NO:602 is the determined cDNA sequence of clone 61219775
25 SEQ ID NO:603 is the determined cDNA sequence of clone 61220056
SEQ ID NO:604 is the determined cDNA sequence of clone 61220058
SEQ ID NO:605 is the determined cDNA sequence of clone 61220059
SEQ ID NO:606 is the determined cDNA sequence of clone 61220060
SEQ ID NO:607 is the determined cDNA sequence of clone 61220062
30 SEQ ID NO:608 is the determined cDNA sequence of clone 61220064
SEQ ID NO:609 is the determined cDNA sequence of clone 61220065

SEQ ID NO:610 is the determined cDNA sequence of clone 61220066
SEQ ID NO:611 is the determined cDNA sequence of clone 61220067
SEQ ID NO:612 is the determined cDNA sequence of clone 61220068
SEQ ID NO:613 is the determined cDNA sequence of clone 61220069
5 SEQ ID NO:614 is the determined cDNA sequence of clone 61220070
SEQ ID NO:615 is the determined cDNA sequence of clone 61220071
SEQ ID NO:616 is the determined cDNA sequence of clone 61220072
SEQ ID NO:617 is the determined cDNA sequence of clone 61220073
SEQ ID NO:618 is the determined cDNA sequence of clone 61220074
10 SEQ ID NO:619 is the determined cDNA sequence of clone 61220075
SEQ ID NO:620 is the determined cDNA sequence of clone 61220076
SEQ ID NO:621 is the determined cDNA sequence of clone 61220077
SEQ ID NO:622 is the determined cDNA sequence of clone 61220078
SEQ ID NO:623 is the determined cDNA sequence of clone 61220080
15 SEQ ID NO:624 is the determined cDNA sequence of clone 61220081
SEQ ID NO:625 is the determined cDNA sequence of clone 61220082
SEQ ID NO:626 is the determined cDNA sequence of clone 61220083
SEQ ID NO:627 is the determined cDNA sequence of clone 61220084
SEQ ID NO:628 is the determined cDNA sequence of clone 61220085
20 SEQ ID NO:629 is the determined cDNA sequence of clone 61220086
SEQ ID NO:630 is the determined cDNA sequence of clone 61220087
SEQ ID NO:631 is the determined cDNA sequence of clone 61220088
SEQ ID NO:632 is the determined cDNA sequence of clone 61220089
SEQ ID NO:633 is the determined cDNA sequence of clone 61220090
25 SEQ ID NO:634 is the determined cDNA sequence of clone 61220091
SEQ ID NO:635 is the determined cDNA sequence of clone 61220093
SEQ ID NO:636 is the determined cDNA sequence of clone 61220094
SEQ ID NO:637 is the determined cDNA sequence of clone 61220095
SEQ ID NO:638 is the determined cDNA sequence of clone 61220096
30 SEQ ID NO:639 is the determined cDNA sequence of clone 61220097
SEQ ID NO:640 is the determined cDNA sequence of clone 61220099

SEQ ID NO:641 is the determined cDNA sequence of clone 61220100
SEQ ID NO:642 is the determined cDNA sequence of clone 61220101
SEQ ID NO:643 is the determined cDNA sequence of clone 61220104
SEQ ID NO:644 is the determined cDNA sequence of clone 61220105
5 SEQ ID NO:645 is the determined cDNA sequence of clone 61220106
SEQ ID NO:646 is the determined cDNA sequence of clone 61220107
SEQ ID NO:647 is the determined cDNA sequence of clone 61220108
SEQ ID NO:648 is the determined cDNA sequence of clone 61220109
SEQ ID NO:649 is the determined cDNA sequence of clone 61220110
10 SEQ ID NO:650 is the determined cDNA sequence of clone 61220112
SEQ ID NO:651 is the determined cDNA sequence of clone 61220113
SEQ ID NO:652 is the determined cDNA sequence of clone 61220114
SEQ ID NO:653 is the determined cDNA sequence of clone 61220115
SEQ ID NO:654 is the determined cDNA sequence of clone 61220116
15 SEQ ID NO:655 is the determined cDNA sequence of clone 61220117
SEQ ID NO:656 is the determined cDNA sequence of clone 61220118
SEQ ID NO:657 is the determined cDNA sequence of clone 61220119
SEQ ID NO:658 is the determined cDNA sequence of clone 61220120
SEQ ID NO:659 is the determined cDNA sequence of clone 61220121
20 SEQ ID NO:660 is the determined cDNA sequence of clone 61220122
SEQ ID NO:661 is the determined cDNA sequence of clone 61220124
SEQ ID NO:662 is the determined cDNA sequence of clone 61220125
SEQ ID NO:663 is the determined cDNA sequence of clone 61220126
SEQ ID NO:664 is the determined cDNA sequence of clone 61220127
25 SEQ ID NO:665 is the determined cDNA sequence of clone 61220128
SEQ ID NO:666 is the determined cDNA sequence of clone 61220129
SEQ ID NO:667 is the determined cDNA sequence of clone 61220130
SEQ ID NO:668 is the determined cDNA sequence of clone 61220133
SEQ ID NO:669 is the determined cDNA sequence of clone 61220134
30 SEQ ID NO:670 is the determined cDNA sequence of clone 61220135
SEQ ID NO:671 is the determined cDNA sequence of clone 61220137

SEQ ID NO:672 is the determined cDNA sequence of clone 61220139
SEQ ID NO:673 is the determined cDNA sequence of clone 61220140
SEQ ID NO:674 is the determined cDNA sequence of clone 61220141
SEQ ID NO:675 is the determined cDNA sequence of clone 61220142
5 SEQ ID NO:676 is the determined cDNA sequence of clone 61220143
SEQ ID NO:677 is the determined cDNA sequence of clone 61220144
SEQ ID NO:678 is the determined cDNA sequence of clone 61220146
SEQ ID NO:679 is the determined cDNA sequence of clone 61220147
SEQ ID NO:680 is the determined cDNA sequence of clone 61219777
10 SEQ ID NO:681 is the determined cDNA sequence of clone 61219778
SEQ ID NO:682 is the determined cDNA sequence of clone 61219779
SEQ ID NO:683 is the determined cDNA sequence of clone 61219780
SEQ ID NO:684 is the determined cDNA sequence of clone 61219781
SEQ ID NO:685 is the determined cDNA sequence of clone 61219782
15 SEQ ID NO:686 is the determined cDNA sequence of clone 61219783
SEQ ID NO:687 is the determined cDNA sequence of clone 61219784
SEQ ID NO:688 is the determined cDNA sequence of clone 61219785
SEQ ID NO:689 is the determined cDNA sequence of clone 61219786
SEQ ID NO:690 is the determined cDNA sequence of clone 61219787
20 SEQ ID NO:691 is the determined cDNA sequence of clone 61219788
SEQ ID NO:692 is the determined cDNA sequence of clone 61219789
SEQ ID NO:693 is the determined cDNA sequence of clone 61219790
SEQ ID NO:694 is the determined cDNA sequence of clone 61219791
SEQ ID NO:695 is the determined cDNA sequence of clone 61219792
25 SEQ ID NO:696 is the determined cDNA sequence of clone 61219793
SEQ ID NO:697 is the determined cDNA sequence of clone 61219794
SEQ ID NO:698 is the determined cDNA sequence of clone 61219795
SEQ ID NO:699 is the determined cDNA sequence of clone 61219797
SEQ ID NO:700 is the determined cDNA sequence of clone 61219798
30 SEQ ID NO:701 is the determined cDNA sequence of clone 61219799
SEQ ID NO:702 is the determined cDNA sequence of clone 61219800

SEQ ID NO:703 is the determined cDNA sequence of clone 61219801
SEQ ID NO:704 is the determined cDNA sequence of clone 61219802
SEQ ID NO:705 is the determined cDNA sequence of clone 61219803
SEQ ID NO:706 is the determined cDNA sequence of clone 61219804
5 SEQ ID NO:707 is the determined cDNA sequence of clone 61219805
SEQ ID NO:708 is the determined cDNA sequence of clone 61219806
SEQ ID NO:709 is the determined cDNA sequence of clone 61219807
SEQ ID NO:710 is the determined cDNA sequence of clone 61219808
SEQ ID NO:711 is the determined cDNA sequence of clone 61219809
10 SEQ ID NO:712 is the determined cDNA sequence of clone 61219810
SEQ ID NO:713 is the determined cDNA sequence of clone 61219812
SEQ ID NO:714 is the determined cDNA sequence of clone 61219814
SEQ ID NO:715 is the determined cDNA sequence of clone 61219815
SEQ ID NO:716 is the determined cDNA sequence of clone 61219816
15 SEQ ID NO:717 is the determined cDNA sequence of clone 61219817
SEQ ID NO:718 is the determined cDNA sequence of clone 61219818
SEQ ID NO:719 is the determined cDNA sequence of clone 61219819
SEQ ID NO:720 is the determined cDNA sequence of clone 61219820
SEQ ID NO:721 is the determined cDNA sequence of clone 61219821
20 SEQ ID NO:722 is the determined cDNA sequence of clone 61219822
SEQ ID NO:723 is the determined cDNA sequence of clone 61219823
SEQ ID NO:724 is the determined cDNA sequence of clone 61219824
SEQ ID NO:725 is the determined cDNA sequence of clone 61219825
SEQ ID NO:726 is the determined cDNA sequence of clone 61219826
25 SEQ ID NO:727 is the determined cDNA sequence of clone 61219827
SEQ ID NO:728 is the determined cDNA sequence of clone 61219828
SEQ ID NO:729 is the determined cDNA sequence of clone 61219829
SEQ ID NO:730 is the determined cDNA sequence of clone 61219830
SEQ ID NO:731 is the determined cDNA sequence of clone 61219831
30 SEQ ID NO:732 is the determined cDNA sequence of clone 61219832
SEQ ID NO:733 is the determined cDNA sequence of clone 61219833

SEQ ID NO:734 is the determined cDNA sequence of clone 61219834
SEQ ID NO:735 is the determined cDNA sequence of clone 61219835
SEQ ID NO:736 is the determined cDNA sequence of clone 61219836
SEQ ID NO:737 is the determined cDNA sequence of clone 61219838
5 SEQ ID NO:738 is the determined cDNA sequence of clone 61219839
SEQ ID NO:739 is the determined cDNA sequence of clone 61219840
SEQ ID NO:740 is the determined cDNA sequence of clone 61219841
SEQ ID NO:741 is the determined cDNA sequence of clone 61219842
SEQ ID NO:742 is the determined cDNA sequence of clone 61219843
10 SEQ ID NO:743 is the determined cDNA sequence of clone 61219844
SEQ ID NO:744 is the determined cDNA sequence of clone 61219845
SEQ ID NO:745 is the determined cDNA sequence of clone 61219846
SEQ ID NO:746 is the determined cDNA sequence of clone 61219848
SEQ ID NO:747 is the determined cDNA sequence of clone 61219850
15 SEQ ID NO:748 is the determined cDNA sequence of clone 61219851
SEQ ID NO:749 is the determined cDNA sequence of clone 61219853
SEQ ID NO:750 is the determined cDNA sequence of clone 61219854
SEQ ID NO:751 is the determined cDNA sequence of clone 61219857
SEQ ID NO:752 is the determined cDNA sequence of clone 61219858
20 SEQ ID NO:753 is the determined cDNA sequence of clone 61219859
SEQ ID NO:754 is the determined cDNA sequence of clone 61219860
SEQ ID NO:755 is the determined cDNA sequence of clone 61219861
SEQ ID NO:756 is the determined cDNA sequence of clone 61219862
SEQ ID NO:757 is the determined cDNA sequence of clone 61219863
25 SEQ ID NO:758 is the determined cDNA sequence of clone 61219864
SEQ ID NO:759 is the determined cDNA sequence of clone 61219865
SEQ ID NO:760 is the determined cDNA sequence of clone 61219866
SEQ ID NO:761 is the determined cDNA sequence of clone 61219867
SEQ ID NO:762 is the determined cDNA sequence of clone 61219869
30 SEQ ID NO:763 is the determined cDNA sequence of clone 61220149
SEQ ID NO:764 is the determined cDNA sequence of clone 61220150

SEQ ID NO:765 is the determined cDNA sequence of clone 61220151
SEQ ID NO:766 is the determined cDNA sequence of clone 61220152
SEQ ID NO:767 is the determined cDNA sequence of clone 61220153
SEQ ID NO:768 is the determined cDNA sequence of clone 61220154
5 SEQ ID NO:769 is the determined cDNA sequence of clone 61220156
SEQ ID NO:770 is the determined cDNA sequence of clone 61220158
SEQ ID NO:771 is the determined cDNA sequence of clone 61220159
SEQ ID NO:772 is the determined cDNA sequence of clone 61220160
SEQ ID NO:773 is the determined cDNA sequence of clone 61220161
10 SEQ ID NO:774 is the determined cDNA sequence of clone 61220162
SEQ ID NO:775 is the determined cDNA sequence of clone 61220163
SEQ ID NO:776 is the determined cDNA sequence of clone 61220164
SEQ ID NO:777 is the determined cDNA sequence of clone 61220167
SEQ ID NO:778 is the determined cDNA sequence of clone 61220168
15 SEQ ID NO:779 is the determined cDNA sequence of clone 61220169
SEQ ID NO:780 is the determined cDNA sequence of clone 61220170
SEQ ID NO:781 is the determined cDNA sequence of clone 61220171
SEQ ID NO:782 is the determined cDNA sequence of clone 61220172
SEQ ID NO:783 is the determined cDNA sequence of clone 61220173
20 SEQ ID NO:784 is the determined cDNA sequence of clone 61220175
SEQ ID NO:785 is the determined cDNA sequence of clone 61220176
SEQ ID NO:786 is the determined cDNA sequence of clone 61220177
SEQ ID NO:787 is the determined cDNA sequence of clone 61220178
SEQ ID NO:788 is the determined cDNA sequence of clone 61220179
25 SEQ ID NO:789 is the determined cDNA sequence of clone 61220180
SEQ ID NO:790 is the determined cDNA sequence of clone 61220181
SEQ ID NO:791 is the determined cDNA sequence of clone 61220182
SEQ ID NO:792 is the determined cDNA sequence of clone 61220183
SEQ ID NO:793 is the determined cDNA sequence of clone 61220184
30 SEQ ID NO:794 is the determined cDNA sequence of clone 61220185
SEQ ID NO:795 is the determined cDNA sequence of clone 61220186

SEQ ID NO:796 is the determined cDNA sequence of clone 61220187
SEQ ID NO:797 is the determined cDNA sequence of clone 61220188
SEQ ID NO:798 is the determined cDNA sequence of clone 61220189
SEQ ID NO:799 is the determined cDNA sequence of clone 61220190
5 SEQ ID NO:800 is the determined cDNA sequence of clone 61220192
SEQ ID NO:801 is the determined cDNA sequence of clone 61220193
SEQ ID NO:802 is the determined cDNA sequence of clone 61220194
SEQ ID NO:803 is the determined cDNA sequence of clone 61220195
SEQ ID NO:804 is the determined cDNA sequence of clone 61220196
10 SEQ ID NO:805 is the determined cDNA sequence of clone 61220198
SEQ ID NO:806 is the determined cDNA sequence of clone 61220199
SEQ ID NO:807 is the determined cDNA sequence of clone 61220200
SEQ ID NO:808 is the determined cDNA sequence of clone 61220203
SEQ ID NO:809 is the determined cDNA sequence of clone 61220204
15 SEQ ID NO:810 is the determined cDNA sequence of clone 61220205
SEQ ID NO:811 is the determined cDNA sequence of clone 61220207
SEQ ID NO:812 is the determined cDNA sequence of clone 61220208
SEQ ID NO:813 is the determined cDNA sequence of clone 61220209
SEQ ID NO:814 is the determined cDNA sequence of clone 61220210
20 SEQ ID NO:815 is the determined cDNA sequence of clone 61220211
SEQ ID NO:816 is the determined cDNA sequence of clone 61220213
SEQ ID NO:817 is the determined cDNA sequence of clone 61220214
SEQ ID NO:818 is the determined cDNA sequence of clone 61220216
SEQ ID NO:819 is the determined cDNA sequence of clone 61220217
25 SEQ ID NO:820 is the determined cDNA sequence of clone 61220219
SEQ ID NO:821 is the determined cDNA sequence of clone 61220220
SEQ ID NO:822 is the determined cDNA sequence of clone 61220221
SEQ ID NO:823 is the determined cDNA sequence of clone 61220222
SEQ ID NO:824 is the determined cDNA sequence of clone 61220223
30 SEQ ID NO:825 is the determined cDNA sequence of clone 61220224
SEQ ID NO:826 is the determined cDNA sequence of clone 61220225

SEQ ID NO:827 is the determined cDNA sequence of clone 61220226
SEQ ID NO:828 is the determined cDNA sequence of clone 61220227
SEQ ID NO:829 is the determined cDNA sequence of clone 61220228
SEQ ID NO:830 is the determined cDNA sequence of clone 61220230
5 SEQ ID NO:831 is the determined cDNA sequence of clone 61220231
SEQ ID NO:832 is the determined cDNA sequence of clone 61220232
SEQ ID NO:833 is the determined cDNA sequence of clone 61220233
SEQ ID NO:834 is the determined cDNA sequence of clone 61220234
SEQ ID NO:835 is the determined cDNA sequence of clone 61220235
10 SEQ ID NO:836 is the determined cDNA sequence of clone 61220236
SEQ ID NO:837 is the determined cDNA sequence of clone 61220237
SEQ ID NO:838 is the determined cDNA sequence of clone 61220239
SEQ ID NO:839 is the determined cDNA sequence of clone 61220240
SEQ ID NO:840 is the determined cDNA sequence of clone 61220241
15 SEQ ID NO:841 is the determined cDNA sequence of clone 61220242
SEQ ID NO:842 is the determined cDNA sequence of clone 61220244
SEQ ID NO:843 is the determined cDNA sequence of clone 61220245
SEQ ID NO:844 is the determined cDNA sequence of clone 61220246
SEQ ID NO:845 is the determined cDNA sequence of clone 61220247
20 SEQ ID NO:846 is the determined cDNA sequence of clone 61220248
SEQ ID NO:847 is the determined cDNA sequence of clone 61220249
SEQ ID NO:848 is the determined cDNA sequence of clone 61220250
SEQ ID NO:849 is the determined cDNA sequence of clone 61220251
SEQ ID NO:850 is the determined cDNA sequence of clone 61220252
25 SEQ ID NO:851 is the determined cDNA sequence of clone 61220253
SEQ ID NO:852 is the determined cDNA sequence of clone 61220254
SEQ ID NO:853 is the determined cDNA sequence of clone 61220255
SEQ ID NO:854 is the determined cDNA sequence of clone 61220256
SEQ ID NO:855 is the determined cDNA sequence of clone 61220258
30 SEQ ID NO:856 is the determined cDNA sequence of clone 61220259
SEQ ID NO:857 is the determined cDNA sequence of clone 61220260

SEQ ID NO:858 is the determined cDNA sequence of clone 61220261
SEQ ID NO:859 is the determined cDNA sequence of clone 61220262
SEQ ID NO:860 is the determined cDNA sequence of clone 61220263
SEQ ID NO:861 is the determined cDNA sequence of clone 61220264
5 SEQ ID NO:862 is the determined cDNA sequence of clone 61220265
SEQ ID NO:863 is the determined cDNA sequence of clone 61220267
SEQ ID NO:864 is the determined cDNA sequence of clone 61220268
SEQ ID NO:865 is the determined cDNA sequence of clone 61220269
SEQ ID NO:866 is the determined cDNA sequence of clone 61220270
10 SEQ ID NO:867 is the determined cDNA sequence of clone 61220271
SEQ ID NO:868 is the determined cDNA sequence of clone 61220272
SEQ ID NO:869 is the determined cDNA sequence of clone 61220273
SEQ ID NO:870 is the determined cDNA sequence of clone 61220274
SEQ ID NO:871 is the determined cDNA sequence of clone 61220275
15 SEQ ID NO:872 is the determined cDNA sequence of clone 61220278
SEQ ID NO:873 is the determined cDNA sequence of clone 61220279
SEQ ID NO:874 is the determined cDNA sequence of clone 61220280
SEQ ID NO:875 is the determined cDNA sequence of clone 61220281
SEQ ID NO:876 is the determined cDNA sequence of clone 61220282
20 SEQ ID NO:877 is the determined cDNA sequence of clone 61220283
SEQ ID NO:878 is the determined cDNA sequence of clone 61220284
SEQ ID NO:879 is the determined cDNA sequence of clone 61220285
SEQ ID NO:880 is the determined cDNA sequence of clone 61220287
SEQ ID NO:881 is the determined cDNA sequence of clone 61220288
25 SEQ ID NO:882 is the determined cDNA sequence of clone 61220290
SEQ ID NO:883 is the determined cDNA sequence of clone 61220291
SEQ ID NO:884 is the determined cDNA sequence of clone 61220292
SEQ ID NO:885 is the determined cDNA sequence of clone 61220293
SEQ ID NO:886 is the determined cDNA sequence of clone 61220294
30 SEQ ID NO:887 is the determined cDNA sequence of clone 61220295
SEQ ID NO:888 is the determined cDNA sequence of clone 61220296

SEQ ID NO:889 is the determined cDNA sequence of clone 61220298
SEQ ID NO:890 is the determined cDNA sequence of clone 61220299
SEQ ID NO:891 is the determined cDNA sequence of clone 61220300
SEQ ID NO:892 is the determined cDNA sequence of clone 61220301
5 SEQ ID NO:893 is the determined cDNA sequence of clone 61220302
SEQ ID NO:894 is the determined cDNA sequence of clone 61220303
SEQ ID NO:895 is the determined cDNA sequence of clone 61220304
SEQ ID NO:896 is the determined cDNA sequence of clone 61220305
SEQ ID NO:897 is the determined cDNA sequence of clone 61220307
10 SEQ ID NO:898 is the determined cDNA sequence of clone 61220308
SEQ ID NO:899 is the determined cDNA sequence of clone 61220309
SEQ ID NO:900 is the determined cDNA sequence of clone 61220310
SEQ ID NO:901 is the determined cDNA sequence of clone 61220314
SEQ ID NO:902 is the determined cDNA sequence of clone 61220316
15 SEQ ID NO:903 is the determined cDNA sequence of clone 61220317
SEQ ID NO:904 is the determined cDNA sequence of clone 61220318
SEQ ID NO:905 is the determined cDNA sequence of clone 61220319
SEQ ID NO:906 is the determined cDNA sequence of clone 61220320
SEQ ID NO:907 is the determined cDNA sequence of clone 61220321
20 SEQ ID NO:908 is the determined cDNA sequence of clone 61220322
SEQ ID NO:909 is the determined cDNA sequence of clone 61220323
SEQ ID NO:910 is the determined cDNA sequence of clone 61220324
SEQ ID NO:911 is the determined cDNA sequence of clone 61220325
SEQ ID NO:912 is the determined cDNA sequence of clone 61220327
25 SEQ ID NO:913 is the determined cDNA sequence of clone 61220328
SEQ ID NO:914 is the determined cDNA sequence of clone 61220330
SEQ ID NO:915 is the determined cDNA sequence of clone 61220331
SEQ ID NO:916 is the determined cDNA sequence of clone 61220332
SEQ ID NO:917 is the determined cDNA sequence of clone 61220333
30 SEQ ID NO:918 is the determined cDNA sequence of clone 61220334
SEQ ID NO:919 is the determined cDNA sequence of clone 61219870

SEQ ID NO:920 is the determined cDNA sequence of clone 61219871
SEQ ID NO:921 is the determined cDNA sequence of clone 61219872
SEQ ID NO:922 is the determined cDNA sequence of clone 61219874
SEQ ID NO:923 is the determined cDNA sequence of clone 61219875
5 SEQ ID NO:924 is the determined cDNA sequence of clone 61219877
SEQ ID NO:925 is the determined cDNA sequence of clone 61219878
SEQ ID NO:926 is the determined cDNA sequence of clone 61219879
SEQ ID NO:927 is the determined cDNA sequence of clone 61219880
SEQ ID NO:928 is the determined cDNA sequence of clone 61219881
10 SEQ ID NO:929 is the determined cDNA sequence of clone 61219882
SEQ ID NO:930 is the determined cDNA sequence of clone 61219883
SEQ ID NO:931 is the determined cDNA sequence of clone 61219884
SEQ ID NO:932 is the determined cDNA sequence of clone 61219885
SEQ ID NO:933 is the determined cDNA sequence of clone 61219886
15 SEQ ID NO:934 is the determined cDNA sequence of clone 61219887
SEQ ID NO:935 is the determined cDNA sequence of clone 61219888
SEQ ID NO:936 is the determined cDNA sequence of clone 61219889
SEQ ID NO:937 is the determined cDNA sequence of clone 61219892
SEQ ID NO:938 is the determined cDNA sequence of clone 61219893
20 SEQ ID NO:939 is the determined cDNA sequence of clone 61219894
SEQ ID NO:940 is the determined cDNA sequence of clone 61219895
SEQ ID NO:941 is the determined cDNA sequence of clone 61219897
SEQ ID NO:942 is the determined cDNA sequence of clone 61219898
SEQ ID NO:943 is the determined cDNA sequence of clone 61219899
25 SEQ ID NO:944 is the determined cDNA sequence of clone 61219900
SEQ ID NO:945 is the determined cDNA sequence of clone 61219901
SEQ ID NO:946 is the determined cDNA sequence of clone 61219902
SEQ ID NO:947 is the determined cDNA sequence of clone 61219903
SEQ ID NO:948 is the determined cDNA sequence of clone 61219905
30 SEQ ID NO:949 is the determined cDNA sequence of clone 61219906
SEQ ID NO:950 is the determined cDNA sequence of clone 61219907

SEQ ID NO:951 is the determined cDNA sequence of clone 61219908
SEQ ID NO:952 is the determined cDNA sequence of clone 61219909
SEQ ID NO:953 is the determined cDNA sequence of clone 61219910
SEQ ID NO:954 is the determined cDNA sequence of clone 61219911
5 SEQ ID NO:955 is the determined cDNA sequence of clone 61219912
SEQ ID NO:956 is the determined cDNA sequence of clone 61219914
SEQ ID NO:957 is the determined cDNA sequence of clone 61219915
SEQ ID NO:958 is the determined cDNA sequence of clone 61219916
SEQ ID NO:959 is the determined cDNA sequence of clone 61219917
10 SEQ ID NO:960 is the determined cDNA sequence of clone 61219918
SEQ ID NO:961 is the determined cDNA sequence of clone 61219919
SEQ ID NO:962 is the determined cDNA sequence of clone 61219920
SEQ ID NO:963 is the determined cDNA sequence of clone 61219921
SEQ ID NO:964 is the determined cDNA sequence of clone 61219922
15 SEQ ID NO:965 is the determined cDNA sequence of clone 61219923
SEQ ID NO:966 is the determined cDNA sequence of clone 61219927
SEQ ID NO:967 is the determined cDNA sequence of clone 61219928
SEQ ID NO:968 is the determined cDNA sequence of clone 61219929
SEQ ID NO:969 is the determined cDNA sequence of clone 61219932
20 SEQ ID NO:970 is the determined cDNA sequence of clone 61219933
SEQ ID NO:971 is the determined cDNA sequence of clone 61219934
SEQ ID NO:972 is the determined cDNA sequence of clone 61219935
SEQ ID NO:973 is the determined cDNA sequence of clone 61219936
SEQ ID NO:974 is the determined cDNA sequence of clone 61219937
25 SEQ ID NO:975 is the determined cDNA sequence of clone 61219938
SEQ ID NO:976 is the determined cDNA sequence of clone 61219940
SEQ ID NO:977 is the determined cDNA sequence of clone 61219941
SEQ ID NO:978 is the determined cDNA sequence of clone 61219942
SEQ ID NO:979 is the determined cDNA sequence of clone 61219943
30 SEQ ID NO:980 is the determined cDNA sequence of clone 61219944
SEQ ID NO:981 is the determined cDNA sequence of clone 61219946

SEQ ID NO:982 is the determined cDNA sequence of clone 61219947
SEQ ID NO:983 is the determined cDNA sequence of clone 61219948
SEQ ID NO:984 is the determined cDNA sequence of clone 61219949
SEQ ID NO:985 is the determined cDNA sequence of clone 61219951
5 SEQ ID NO:986 is the determined cDNA sequence of clone 61219952
SEQ ID NO:987 is the determined cDNA sequence of clone 61219953
SEQ ID NO:988 is the determined cDNA sequence of clone 61219955
SEQ ID NO:989 is the determined cDNA sequence of clone 61219956
SEQ ID NO:990 is the determined cDNA sequence of clone 61219957
10 SEQ ID NO:991 is the determined cDNA sequence of clone 61219959
SEQ ID NO:992 is the determined cDNA sequence of clone 61219961
SEQ ID NO:993 is the determined cDNA sequence of clone 61219962
SEQ ID NO:994 is the determined cDNA sequence of clone 61220338
SEQ ID NO:995 is the determined cDNA sequence of clone 61220339
15 SEQ ID NO:996 is the determined cDNA sequence of clone 61220340
SEQ ID NO:997 is the determined cDNA sequence of clone 61220341
SEQ ID NO:998 is the determined cDNA sequence of clone 61220342
SEQ ID NO:999 is the determined cDNA sequence of clone 61220343
SEQ ID NO:1000 is the determined cDNA sequence of clone 61220344
20 SEQ ID NO:1001 is the determined cDNA sequence of clone 61220345
SEQ ID NO:1002 is the determined cDNA sequence of clone 61220346
SEQ ID NO:1003 is the determined cDNA sequence of clone 61220347
SEQ ID NO:1004 is the determined cDNA sequence of clone 61220348
SEQ ID NO:1005 is the determined cDNA sequence of clone 61220349
25 SEQ ID NO:1006 is the determined cDNA sequence of clone 61220350
SEQ ID NO:1007 is the determined cDNA sequence of clone 61220351
SEQ ID NO:1008 is the determined cDNA sequence of clone 61220352
SEQ ID NO:1009 is the determined cDNA sequence of clone 61220353
SEQ ID NO:1010 is the determined cDNA sequence of clone 61220354
30 SEQ ID NO:1011 is the determined cDNA sequence of clone 61220356
SEQ ID NO:1012 is the determined cDNA sequence of clone 61220357

SEQ ID NO:1013 is the determined cDNA sequence of clone 61220358
SEQ ID NO:1014 is the determined cDNA sequence of clone 61220359
SEQ ID NO:1015 is the determined cDNA sequence of clone 61220360
SEQ ID NO:1016 is the determined cDNA sequence of clone 61220361
5 SEQ ID NO:1017 is the determined cDNA sequence of clone 61220362
SEQ ID NO:1018 is the determined cDNA sequence of clone 61220363
SEQ ID NO:1019 is the determined cDNA sequence of clone 61220364
SEQ ID NO:1020 is the determined cDNA sequence of clone 61220365
SEQ ID NO:1021 is the determined cDNA sequence of clone 61220366
10 SEQ ID NO:1022 is the determined cDNA sequence of clone 61220367
SEQ ID NO:1023 is the determined cDNA sequence of clone 61220368
SEQ ID NO:1024 is the determined cDNA sequence of clone 61220369
SEQ ID NO:1025 is the determined cDNA sequence of clone 61220370
SEQ ID NO:1026 is the determined cDNA sequence of clone 61220372
15 SEQ ID NO:1027 is the determined cDNA sequence of clone 61220373
SEQ ID NO:1028 is the determined cDNA sequence of clone 61220374
SEQ ID NO:1029 is the determined cDNA sequence of clone 61220375
SEQ ID NO:1030 is the determined cDNA sequence of clone 61220376
SEQ ID NO:1031 is the determined cDNA sequence of clone 61220377
20 SEQ ID NO:1032 is the determined cDNA sequence of clone 61220378
SEQ ID NO:1033 is the determined cDNA sequence of clone 61220380
SEQ ID NO:1034 is the determined cDNA sequence of clone 61220381
SEQ ID NO:1035 is the determined cDNA sequence of clone 61220382
SEQ ID NO:1036 is the determined cDNA sequence of clone 61220383
25 SEQ ID NO:1037 is the determined cDNA sequence of clone 61220385
SEQ ID NO:1038 is the determined cDNA sequence of clone 61220386
SEQ ID NO:1039 is the determined cDNA sequence of clone 61220387
SEQ ID NO:1040 is the determined cDNA sequence of clone 61220388
SEQ ID NO:1041 is the determined cDNA sequence of clone 61220389
30 SEQ ID NO:1042 is the determined cDNA sequence of clone 61220390
SEQ ID NO:1043 is the determined cDNA sequence of clone 61220391

SEQ ID NO:1044 is the determined cDNA sequence of clone 61220392
SEQ ID NO:1045 is the determined cDNA sequence of clone 61220393
SEQ ID NO:1046 is the determined cDNA sequence of clone 61220394
SEQ ID NO:1047 is the determined cDNA sequence of clone 61220395
5 SEQ ID NO:1048 is the determined cDNA sequence of clone 61220396
SEQ ID NO:1049 is the determined cDNA sequence of clone 61220398
SEQ ID NO:1050 is the determined cDNA sequence of clone 61220399
SEQ ID NO:1051 is the determined cDNA sequence of clone 61220402
SEQ ID NO:1052 is the determined cDNA sequence of clone 61220403
10 SEQ ID NO:1053 is the determined cDNA sequence of clone 61220404
SEQ ID NO:1054 is the determined cDNA sequence of clone 61220405
SEQ ID NO:1055 is the determined cDNA sequence of clone 61220406
SEQ ID NO:1056 is the determined cDNA sequence of clone 61220407
SEQ ID NO:1057 is the determined cDNA sequence of clone 61220408
15 SEQ ID NO:1058 is the determined cDNA sequence of clone 61220409
SEQ ID NO:1059 is the determined cDNA sequence of clone 61220410
SEQ ID NO:1060 is the determined cDNA sequence of clone 61220411
SEQ ID NO:1061 is the determined cDNA sequence of clone 61220413
SEQ ID NO:1062 is the determined cDNA sequence of clone 61220414
20 SEQ ID NO:1063 is the determined cDNA sequence of clone 61220415
SEQ ID NO:1064 is the determined cDNA sequence of clone 61220418
SEQ ID NO:1065 is the determined cDNA sequence of clone 61220419
SEQ ID NO:1066 is the determined cDNA sequence of clone 61220421
SEQ ID NO:1067 is the determined cDNA sequence of clone 61220422
25 SEQ ID NO:1068 is the determined cDNA sequence of clone 61220423
SEQ ID NO:1069 is the determined cDNA sequence of clone 61220424
SEQ ID NO:1070 is the determined cDNA sequence of clone 61220426
SEQ ID NO:1071 is the determined cDNA sequence of clone 61220427
SEQ ID NO:1072 is the determined cDNA sequence of clone 61219963
30 SEQ ID NO:1073 is the determined cDNA sequence of clone 61219964
SEQ ID NO:1074 is the determined cDNA sequence of clone 61219966

SEQ ID NO:1075 is the determined cDNA sequence of clone 61219967
SEQ ID NO:1076 is the determined cDNA sequence of clone 61219968
SEQ ID NO:1077 is the determined cDNA sequence of clone 61219969
SEQ ID NO:1078 is the determined cDNA sequence of clone 61219970
5 SEQ ID NO:1079 is the determined cDNA sequence of clone 61219971
SEQ ID NO:1080 is the determined cDNA sequence of clone 61219973
SEQ ID NO:1081 is the determined cDNA sequence of clone 61219974
SEQ ID NO:1082 is the determined cDNA sequence of clone 61219975
SEQ ID NO:1083 is the determined cDNA sequence of clone 61219978
10 SEQ ID NO:1084 is the determined cDNA sequence of clone 61219979
SEQ ID NO:1085 is the determined cDNA sequence of clone 61219980
SEQ ID NO:1086 is the determined cDNA sequence of clone 61219981
SEQ ID NO:1087 is the determined cDNA sequence of clone 61219982
SEQ ID NO:1088 is the determined cDNA sequence of clone 61219983
15 SEQ ID NO:1089 is the determined cDNA sequence of clone 61219984
SEQ ID NO:1090 is the determined cDNA sequence of clone 61219985
SEQ ID NO:1091 is the determined cDNA sequence of clone 61219986
SEQ ID NO:1092 is the determined cDNA sequence of clone 61219987
SEQ ID NO:1093 is the determined cDNA sequence of clone 61219988
20 SEQ ID NO:1094 is the determined cDNA sequence of clone 61219990
SEQ ID NO:1095 is the determined cDNA sequence of clone 61219991
SEQ ID NO:1096 is the determined cDNA sequence of clone 61219992
SEQ ID NO:1097 is the determined cDNA sequence of clone 61219993
SEQ ID NO:1098 is the determined cDNA sequence of clone 61219994
25 SEQ ID NO:1099 is the determined cDNA sequence of clone 61219995
SEQ ID NO:1100 is the determined cDNA sequence of clone 61219996
SEQ ID NO:1101 is the determined cDNA sequence of clone 61219997
SEQ ID NO:1102 is the determined cDNA sequence of clone 61219999
SEQ ID NO:1103 is the determined cDNA sequence of clone 61220000
30 SEQ ID NO:1104 is the determined cDNA sequence of clone 61220001
SEQ ID NO:1105 is the determined cDNA sequence of clone 61220002

SEQ ID NO:1106 is the determined cDNA sequence of clone 61220003
SEQ ID NO:1107 is the determined cDNA sequence of clone 61220004
SEQ ID NO:1108 is the determined cDNA sequence of clone 61220005
SEQ ID NO:1109 is the determined cDNA sequence of clone 61220006
5 SEQ ID NO:1110 is the determined cDNA sequence of clone 61220007
SEQ ID NO:1111 is the determined cDNA sequence of clone 61220008
SEQ ID NO:1112 is the determined cDNA sequence of clone 61220009
SEQ ID NO:1113 is the determined cDNA sequence of clone 61220011
SEQ ID NO:1114 is the determined cDNA sequence of clone 61220012
10 SEQ ID NO:1115 is the determined cDNA sequence of clone 61220014
SEQ ID NO:1116 is the determined cDNA sequence of clone 61220015
SEQ ID NO:1117 is the determined cDNA sequence of clone 61220016
SEQ ID NO:1118 is the determined cDNA sequence of clone 61220017
SEQ ID NO:1119 is the determined cDNA sequence of clone 61220018
15 SEQ ID NO:1120 is the determined cDNA sequence of clone 61220020
SEQ ID NO:1121 is the determined cDNA sequence of clone 61220022
SEQ ID NO:1122 is the determined cDNA sequence of clone 61220023
SEQ ID NO:1123 is the determined cDNA sequence of clone 61220025
SEQ ID NO:1124 is the determined cDNA sequence of clone 61220026
20 SEQ ID NO:1125 is the determined cDNA sequence of clone 61220027
SEQ ID NO:1126 is the determined cDNA sequence of clone 61220028
SEQ ID NO:1127 is the determined cDNA sequence of clone 61220029
SEQ ID NO:1128 is the determined cDNA sequence of clone 61220032
SEQ ID NO:1129 is the determined cDNA sequence of clone 61220033
25 SEQ ID NO:1130 is the determined cDNA sequence of clone 61220034
SEQ ID NO:1131 is the determined cDNA sequence of clone 61220035
SEQ ID NO:1132 is the determined cDNA sequence of clone 61220036
SEQ ID NO:1133 is the determined cDNA sequence of clone 61220037
SEQ ID NO:1134 is the determined cDNA sequence of clone 61220038
30 SEQ ID NO:1135 is the determined cDNA sequence of clone 61220040
SEQ ID NO:1136 is the determined cDNA sequence of clone 61220043

SEQ ID NO:1137 is the determined cDNA sequence of clone 61220044
SEQ ID NO:1138 is the determined cDNA sequence of clone 61220045
SEQ ID NO:1139 is the determined cDNA sequence of clone 61220046
SEQ ID NO:1140 is the determined cDNA sequence of clone 61220051
5 SEQ ID NO:1141 is the determined cDNA sequence of clone 61220052
SEQ ID NO:1142 is the determined cDNA sequence of clone 61220053
SEQ ID NO:1143 is the determined cDNA sequence of clone 61220054
SEQ ID NO:1144 is the determined cDNA sequence of clone 61220055
SEQ ID NO:1145 is the determined cDNA sequence of clone 61546633
10 SEQ ID NO:1146 is the determined cDNA sequence of clone 61546634
SEQ ID NO:1147 is the determined cDNA sequence of clone 61546635
SEQ ID NO:1148 is the determined cDNA sequence of clone 61546636
SEQ ID NO:1149 is the determined cDNA sequence of clone 61546637
SEQ ID NO:1150 is the determined cDNA sequence of clone 61546639
15 SEQ ID NO:1151 is the determined cDNA sequence of clone 61546642
SEQ ID NO:1152 is the determined cDNA sequence of clone 61546643
SEQ ID NO:1153 is the determined cDNA sequence of clone 61546644
SEQ ID NO:1154 is the determined cDNA sequence of clone 61546645
SEQ ID NO:1155 is the determined cDNA sequence of clone 61546646
20 SEQ ID NO:1156 is the determined cDNA sequence of clone 61546647
SEQ ID NO:1157 is the determined cDNA sequence of clone 61546648
SEQ ID NO:1158 is the determined cDNA sequence of clone 61546649
SEQ ID NO:1159 is the determined cDNA sequence of clone 61546650
SEQ ID NO:1160 is the determined cDNA sequence of clone 61546651
25 SEQ ID NO:1161 is the determined cDNA sequence of clone 61546652
SEQ ID NO:1162 is the determined cDNA sequence of clone 61546653
SEQ ID NO:1163 is the determined cDNA sequence of clone 61546654
SEQ ID NO:1164 is the determined cDNA sequence of clone 61546656
SEQ ID NO:1165 is the determined cDNA sequence of clone 61546657
30 SEQ ID NO:1166 is the determined cDNA sequence of clone 61546658
SEQ ID NO:1167 is the determined cDNA sequence of clone 61546659

SEQ ID NO:1168 is the determined cDNA sequence of clone 61546660
SEQ ID NO:1169 is the determined cDNA sequence of clone 61546661
SEQ ID NO:1170 is the determined cDNA sequence of clone 61546662
SEQ ID NO:1171 is the determined cDNA sequence of clone 61546663
5 SEQ ID NO:1172 is the determined cDNA sequence of clone 61546664
SEQ ID NO:1173 is the determined cDNA sequence of clone 61546665
SEQ ID NO:1174 is the determined cDNA sequence of clone 61546667
SEQ ID NO:1175 is the determined cDNA sequence of clone 61546668
SEQ ID NO:1176 is the determined cDNA sequence of clone 61546669
10 SEQ ID NO:1177 is the determined cDNA sequence of clone 61546670
SEQ ID NO:1178 is the determined cDNA sequence of clone 61546671
SEQ ID NO:1179 is the determined cDNA sequence of clone 61546672
SEQ ID NO:1180 is the determined cDNA sequence of clone 61546674
SEQ ID NO:1181 is the determined cDNA sequence of clone 61546675
15 SEQ ID NO:1182 is the determined cDNA sequence of clone 61546676
SEQ ID NO:1183 is the determined cDNA sequence of clone 61546677
SEQ ID NO:1184 is the determined cDNA sequence of clone 61546679
SEQ ID NO:1185 is the determined cDNA sequence of clone 61546680
SEQ ID NO:1186 is the determined cDNA sequence of clone 61546682
20 SEQ ID NO:1187 is the determined cDNA sequence of clone 61546683
SEQ ID NO:1188 is the determined cDNA sequence of clone 61546684
SEQ ID NO:1189 is the determined cDNA sequence of clone 61546685
SEQ ID NO:1190 is the determined cDNA sequence of clone 61546686
SEQ ID NO:1191 is the determined cDNA sequence of clone 61546687
25 SEQ ID NO:1192 is the determined cDNA sequence of clone 61546688
SEQ ID NO:1193 is the determined cDNA sequence of clone 61546689
SEQ ID NO:1194 is the determined cDNA sequence of clone 61546690
SEQ ID NO:1195 is the determined cDNA sequence of clone 61546691
SEQ ID NO:1196 is the determined cDNA sequence of clone 61546692
30 SEQ ID NO:1197 is the determined cDNA sequence of clone 61546693
SEQ ID NO:1198 is the determined cDNA sequence of clone 61546694

SEQ ID NO:1199 is the determined cDNA sequence of clone 61546695
SEQ ID NO:1200 is the determined cDNA sequence of clone 61546697
SEQ ID NO:1201 is the determined cDNA sequence of clone 61546698
SEQ ID NO:1202 is the determined cDNA sequence of clone 61546699
5 SEQ ID NO:1203 is the determined cDNA sequence of clone 61546700
SEQ ID NO:1204 is the determined cDNA sequence of clone 61546701
SEQ ID NO:1205 is the determined cDNA sequence of clone 61546702
SEQ ID NO:1206 is the determined cDNA sequence of clone 61546703
SEQ ID NO:1207 is the determined cDNA sequence of clone 61546704
10 SEQ ID NO:1208 is the determined cDNA sequence of clone 61546705
SEQ ID NO:1209 is the determined cDNA sequence of clone 61546706
SEQ ID NO:1210 is the determined cDNA sequence of clone 61546707
SEQ ID NO:1211 is the determined cDNA sequence of clone 61546708
SEQ ID NO:1212 is the determined cDNA sequence of clone 61546709
15 SEQ ID NO:1213 is the determined cDNA sequence of clone 61546710
SEQ ID NO:1214 is the determined cDNA sequence of clone 61546711
SEQ ID NO:1215 is the determined cDNA sequence of clone 61546712
SEQ ID NO:1216 is the determined cDNA sequence of clone 61546714
SEQ ID NO:1217 is the determined cDNA sequence of clone 61546716
20 SEQ ID NO:1218 is the determined cDNA sequence of clone 61546718
SEQ ID NO:1219 is the determined cDNA sequence of clone 61546719
SEQ ID NO:1220 is the determined cDNA sequence of clone 61546720
SEQ ID NO:1221 is the determined cDNA sequence of clone 61546722
SEQ ID NO:1222 is the determined cDNA sequence of clone 61546724
25 SEQ ID NO:1223 is the determined cDNA sequence of clone 61220428
SEQ ID NO:1224 is the determined cDNA sequence of clone 61220430
SEQ ID NO:1225 is the determined cDNA sequence of clone 61220431
SEQ ID NO:1226 is the determined cDNA sequence of clone 61220432
SEQ ID NO:1227 is the determined cDNA sequence of clone 61220433
30 SEQ ID NO:1228 is the determined cDNA sequence of clone 61220434
SEQ ID NO:1229 is the determined cDNA sequence of clone 61220435

SEQ ID NO:1230 is the determined cDNA sequence of clone 61220436
SEQ ID NO:1231 is the determined cDNA sequence of clone 61220437
SEQ ID NO:1232 is the determined cDNA sequence of clone 61220439
SEQ ID NO:1233 is the determined cDNA sequence of clone 61220440
5 SEQ ID NO:1234 is the determined cDNA sequence of clone 61220441
SEQ ID NO:1235 is the determined cDNA sequence of clone 61220442
SEQ ID NO:1236 is the determined cDNA sequence of clone 61220443
SEQ ID NO:1237 is the determined cDNA sequence of clone 61220444
SEQ ID NO:1238 is the determined cDNA sequence of clone 61220445
10 SEQ ID NO:1239 is the determined cDNA sequence of clone 61220446
SEQ ID NO:1240 is the determined cDNA sequence of clone 61220447
SEQ ID NO:1241 is the determined cDNA sequence of clone 61220448
SEQ ID NO:1242 is the determined cDNA sequence of clone 61220452
SEQ ID NO:1243 is the determined cDNA sequence of clone 61220453
15 SEQ ID NO:1244 is the determined cDNA sequence of clone 61220454
SEQ ID NO:1245 is the determined cDNA sequence of clone 61220455
SEQ ID NO:1246 is the determined cDNA sequence of clone 61220456
SEQ ID NO:1247 is the determined cDNA sequence of clone 61220457
SEQ ID NO:1248 is the determined cDNA sequence of clone 61220458
20 SEQ ID NO:1249 is the determined cDNA sequence of clone 61220459
SEQ ID NO:1250 is the determined cDNA sequence of clone 61220460
SEQ ID NO:1251 is the determined cDNA sequence of clone 61220461
SEQ ID NO:1252 is the determined cDNA sequence of clone 61220462
SEQ ID NO:1253 is the determined cDNA sequence of clone 61220464
25 SEQ ID NO:1254 is the determined cDNA sequence of clone 61220465
SEQ ID NO:1255 is the determined cDNA sequence of clone 61220466
SEQ ID NO:1256 is the determined cDNA sequence of clone 61220467
SEQ ID NO:1257 is the determined cDNA sequence of clone 61220468
SEQ ID NO:1258 is the determined cDNA sequence of clone 61220469
30 SEQ ID NO:1259 is the determined cDNA sequence of clone 61220470
SEQ ID NO:1260 is the determined cDNA sequence of clone 61220471

SEQ ID NO:1261 is the determined cDNA sequence of clone 61220473
SEQ ID NO:1262 is the determined cDNA sequence of clone 61220474
SEQ ID NO:1263 is the determined cDNA sequence of clone 61220475
SEQ ID NO:1264 is the determined cDNA sequence of clone 61220476
5 SEQ ID NO:1265 is the determined cDNA sequence of clone 61220477
SEQ ID NO:1266 is the determined cDNA sequence of clone 61220478
SEQ ID NO:1267 is the determined cDNA sequence of clone 61220480
SEQ ID NO:1268 is the determined cDNA sequence of clone 61220481
SEQ ID NO:1269 is the determined cDNA sequence of clone 61220482
10 SEQ ID NO:1270 is the determined cDNA sequence of clone 61220483
SEQ ID NO:1271 is the determined cDNA sequence of clone 61220484
SEQ ID NO:1272 is the determined cDNA sequence of clone 61220485
SEQ ID NO:1273 is the determined cDNA sequence of clone 61220486
SEQ ID NO:1274 is the determined cDNA sequence of clone 61220487
15 SEQ ID NO:1275 is the determined cDNA sequence of clone 61220488
SEQ ID NO:1276 is the determined cDNA sequence of clone 61220489
SEQ ID NO:1277 is the determined cDNA sequence of clone 61220490
SEQ ID NO:1278 is the determined cDNA sequence of clone 61220491
SEQ ID NO:1279 is the determined cDNA sequence of clone 61220492
20 SEQ ID NO:1280 is the determined cDNA sequence of clone 61220493
SEQ ID NO:1281 is the determined cDNA sequence of clone 61220494
SEQ ID NO:1282 is the determined cDNA sequence of clone 61220495
SEQ ID NO:1283 is the determined cDNA sequence of clone 61220496
SEQ ID NO:1284 is the determined cDNA sequence of clone 61220497
25 SEQ ID NO:1285 is the determined cDNA sequence of clone 61220498
SEQ ID NO:1286 is the determined cDNA sequence of clone 61220499
SEQ ID NO:1287 is the determined cDNA sequence of clone 61220500
SEQ ID NO:1288 is the determined cDNA sequence of clone 61220501
SEQ ID NO:1289 is the determined cDNA sequence of clone 61220502
30 SEQ ID NO:1290 is the determined cDNA sequence of clone 61220503
SEQ ID NO:1291 is the determined cDNA sequence of clone 61220504

SEQ ID NO:1292 is the determined cDNA sequence of clone 61220505
SEQ ID NO:1293 is the determined cDNA sequence of clone 61220506
SEQ ID NO:1294 is the determined cDNA sequence of clone 61220507
SEQ ID NO:1295 is the determined cDNA sequence of clone 61220508
5 SEQ ID NO:1296 is the determined cDNA sequence of clone 61220509
SEQ ID NO:1297 is the determined cDNA sequence of clone 61220511
SEQ ID NO:1298 is the determined cDNA sequence of clone 61220512
SEQ ID NO:1299 is the determined cDNA sequence of clone 61220513
SEQ ID NO:1300 is the determined cDNA sequence of clone 61220514
10 SEQ ID NO:1301 is the determined cDNA sequence of clone 61220515
SEQ ID NO:1302 is the determined cDNA sequence of clone 61220516
SEQ ID NO:1303 is the determined cDNA sequence of clone 61220517
SEQ ID NO:1304 is the determined cDNA sequence of clone 61220518
SEQ ID NO:1305 is the determined cDNA sequence of clone 61220519
15 SEQ ID NO:1306 is the determined cDNA sequence of clone 61220520
SEQ ID NO:1307 is the determined cDNA sequence of clone 61547443
SEQ ID NO:1308 is the determined cDNA sequence of clone 61547444
SEQ ID NO:1309 is the determined cDNA sequence of clone 61547445
SEQ ID NO:1310 is the determined cDNA sequence of clone 61547446
20 SEQ ID NO:1311 is the determined cDNA sequence of clone 61547447
SEQ ID NO:1312 is the determined cDNA sequence of clone 61547448
SEQ ID NO:1313 is the determined cDNA sequence of clone 61547449
SEQ ID NO:1314 is the determined cDNA sequence of clone 61547451
SEQ ID NO:1315 is the determined cDNA sequence of clone 61547452
25 SEQ ID NO:1316 is the determined cDNA sequence of clone 61547453
SEQ ID NO:1317 is the determined cDNA sequence of clone 61547454
SEQ ID NO:1318 is the determined cDNA sequence of clone 61547455
SEQ ID NO:1319 is the determined cDNA sequence of clone 61547456
SEQ ID NO:1320 is the determined cDNA sequence of clone 61547457
30 SEQ ID NO:1321 is the determined cDNA sequence of clone 61547458
SEQ ID NO:1322 is the determined cDNA sequence of clone 61547459

SEQ ID NO:1323 is the determined cDNA sequence of clone 61547460
SEQ ID NO:1324 is the determined cDNA sequence of clone 61547461
SEQ ID NO:1325 is the determined cDNA sequence of clone 61547462
SEQ ID NO:1326 is the determined cDNA sequence of clone 61547463
5 SEQ ID NO:1327 is the determined cDNA sequence of clone 61547464
SEQ ID NO:1328 is the determined cDNA sequence of clone 61547465
SEQ ID NO:1329 is the determined cDNA sequence of clone 61547466
SEQ ID NO:1330 is the determined cDNA sequence of clone 61547467
SEQ ID NO:1331 is the determined cDNA sequence of clone 61547468
10 SEQ ID NO:1332 is the determined cDNA sequence of clone 61547469
SEQ ID NO:1333 is the determined cDNA sequence of clone 61547470
SEQ ID NO:1334 is the determined cDNA sequence of clone 61547471
SEQ ID NO:1335 is the determined cDNA sequence of clone 61547472
SEQ ID NO:1336 is the determined cDNA sequence of clone 61547473
15 SEQ ID NO:1337 is the determined cDNA sequence of clone 61547474
SEQ ID NO:1338 is the determined cDNA sequence of clone 61547475
SEQ ID NO:1339 is the determined cDNA sequence of clone 61547476
SEQ ID NO:1340 is the determined cDNA sequence of clone 61547477
SEQ ID NO:1341 is the determined cDNA sequence of clone 61547478
20 SEQ ID NO:1342 is the determined cDNA sequence of clone 61547479
SEQ ID NO:1343 is the determined cDNA sequence of clone 61547480
SEQ ID NO:1344 is the determined cDNA sequence of clone 61547481
SEQ ID NO:1345 is the determined cDNA sequence of clone 61547483
SEQ ID NO:1346 is the determined cDNA sequence of clone 61547484
25 SEQ ID NO:1347 is the determined cDNA sequence of clone 61547485
SEQ ID NO:1348 is the determined cDNA sequence of clone 61547486
SEQ ID NO:1349 is the determined cDNA sequence of clone 61547487
SEQ ID NO:1350 is the determined cDNA sequence of clone 61547488
SEQ ID NO:1351 is the determined cDNA sequence of clone 61547489
30 SEQ ID NO:1352 is the determined cDNA sequence of clone 61547490
SEQ ID NO:1353 is the determined cDNA sequence of clone 61547491

SEQ ID NO:1354 is the determined cDNA sequence of clone 61547492
SEQ ID NO:1355 is the determined cDNA sequence of clone 61547494
SEQ ID NO:1356 is the determined cDNA sequence of clone 61547495
SEQ ID NO:1357 is the determined cDNA sequence of clone 61547498
5 SEQ ID NO:1358 is the determined cDNA sequence of clone 61547499
SEQ ID NO:1359 is the determined cDNA sequence of clone 61547500
SEQ ID NO:1360 is the determined cDNA sequence of clone 61547501
SEQ ID NO:1361 is the determined cDNA sequence of clone 61547502
SEQ ID NO:1362 is the determined cDNA sequence of clone 61547503
10 SEQ ID NO:1363 is the determined cDNA sequence of clone 61547504
SEQ ID NO:1364 is the determined cDNA sequence of clone 61547505
SEQ ID NO:1365 is the determined cDNA sequence of clone 61547507
SEQ ID NO:1366 is the determined cDNA sequence of clone 61547508
SEQ ID NO:1367 is the determined cDNA sequence of clone 61547509
15 SEQ ID NO:1368 is the determined cDNA sequence of clone 61547510
SEQ ID NO:1369 is the determined cDNA sequence of clone 61547511
SEQ ID NO:1370 is the determined cDNA sequence of clone 61547512
SEQ ID NO:1371 is the determined cDNA sequence of clone 61547513
SEQ ID NO:1372 is the determined cDNA sequence of clone 61547514
20 SEQ ID NO:1373 is the determined cDNA sequence of clone 61547515
SEQ ID NO:1374 is the determined cDNA sequence of clone 61547516
SEQ ID NO:1375 is the determined cDNA sequence of clone 61547517
SEQ ID NO:1376 is the determined cDNA sequence of clone 61547518
SEQ ID NO:1377 is the determined cDNA sequence of clone 61547519
25 SEQ ID NO:1378 is the determined cDNA sequence of clone 61547520
SEQ ID NO:1379 is the determined cDNA sequence of clone 61547522
SEQ ID NO:1380 is the determined cDNA sequence of clone 61547523
SEQ ID NO:1381 is the determined cDNA sequence of clone 61547524
SEQ ID NO:1382 is the determined cDNA sequence of clone 61547525
30 SEQ ID NO:1383 is the determined cDNA sequence of clone 61547526
SEQ ID NO:1384 is the determined cDNA sequence of clone 61547527

SEQ ID NO:1385 is the determined cDNA sequence of clone 61547528
SEQ ID NO:1386 is the determined cDNA sequence of clone 61547529
SEQ ID NO:1387 is the determined cDNA sequence of clone 61547530
SEQ ID NO:1388 is the determined cDNA sequence of clone 61547532
5 SEQ ID NO:1389 is the determined cDNA sequence of clone 61547533
SEQ ID NO:1390 is the determined cDNA sequence of clone 61547534
SEQ ID NO:1391 is the determined cDNA sequence of clone 61547535
SEQ ID NO:1392 is the determined cDNA sequence of clone 61438573
SEQ ID NO:1393 is the determined cDNA sequence of clone 61438574
10 SEQ ID NO:1394 is the determined cDNA sequence of clone 61438575
SEQ ID NO:1395 is the determined cDNA sequence of clone 61438576
SEQ ID NO:1396 is the determined cDNA sequence of clone 61438577
SEQ ID NO:1397 is the determined cDNA sequence of clone 61438579
SEQ ID NO:1398 is the determined cDNA sequence of clone 61438581
15 SEQ ID NO:1399 is the determined cDNA sequence of clone 61438582
SEQ ID NO:1400 is the determined cDNA sequence of clone 61438583
SEQ ID NO:1401 is the determined cDNA sequence of clone 61438584
SEQ ID NO:1402 is the determined cDNA sequence of clone 61438585
SEQ ID NO:1403 is the determined cDNA sequence of clone 61438586
20 SEQ ID NO:1404 is the determined cDNA sequence of clone 61438588
SEQ ID NO:1405 is the determined cDNA sequence of clone 61438589
SEQ ID NO:1406 is the determined cDNA sequence of clone 61438590
SEQ ID NO:1407 is the determined cDNA sequence of clone 61438591
SEQ ID NO:1408 is the determined cDNA sequence of clone 61438592
25 SEQ ID NO:1409 is the determined cDNA sequence of clone 61438593
SEQ ID NO:1410 is the determined cDNA sequence of clone 61438594
SEQ ID NO:1411 is the determined cDNA sequence of clone 61438595
SEQ ID NO:1412 is the determined cDNA sequence of clone 61438596
SEQ ID NO:1413 is the determined cDNA sequence of clone 61438597
30 SEQ ID NO:1414 is the determined cDNA sequence of clone 61438598
SEQ ID NO:1415 is the determined cDNA sequence of clone 61438599

SEQ ID NO:1416 is the determined cDNA sequence of clone 61438600
SEQ ID NO:1417 is the determined cDNA sequence of clone 61438601
SEQ ID NO:1418 is the determined cDNA sequence of clone 61438602
SEQ ID NO:1419 is the determined cDNA sequence of clone 61438603
5 SEQ ID NO:1420 is the determined cDNA sequence of clone 61438604
SEQ ID NO:1421 is the determined cDNA sequence of clone 61438607
SEQ ID NO:1422 is the determined cDNA sequence of clone 61438608
SEQ ID NO:1423 is the determined cDNA sequence of clone 61438609
SEQ ID NO:1424 is the determined cDNA sequence of clone 61438610
10 SEQ ID NO:1425 is the determined cDNA sequence of clone 61438611
SEQ ID NO:1426 is the determined cDNA sequence of clone 61438612
SEQ ID NO:1427 is the determined cDNA sequence of clone 61438613
SEQ ID NO:1428 is the determined cDNA sequence of clone 61438615
SEQ ID NO:1429 is the determined cDNA sequence of clone 61438616
15 SEQ ID NO:1430 is the determined cDNA sequence of clone 61438617
SEQ ID NO:1431 is the determined cDNA sequence of clone 61438618
SEQ ID NO:1432 is the determined cDNA sequence of clone 61438620
SEQ ID NO:1433 is the determined cDNA sequence of clone 61438621
SEQ ID NO:1434 is the determined cDNA sequence of clone 61438622
20 SEQ ID NO:1435 is the determined cDNA sequence of clone 61438623
SEQ ID NO:1436 is the determined cDNA sequence of clone 61438624
SEQ ID NO:1437 is the determined cDNA sequence of clone 61438625
SEQ ID NO:1438 is the determined cDNA sequence of clone 61438626
SEQ ID NO:1439 is the determined cDNA sequence of clone 61438627
25 SEQ ID NO:1440 is the determined cDNA sequence of clone 61438629
SEQ ID NO:1441 is the determined cDNA sequence of clone 61438630
SEQ ID NO:1442 is the determined cDNA sequence of clone 61438631
SEQ ID NO:1443 is the determined cDNA sequence of clone 61438632
SEQ ID NO:1444 is the determined cDNA sequence of clone 61438633
30 SEQ ID NO:1445 is the determined cDNA sequence of clone 61438634
SEQ ID NO:1446 is the determined cDNA sequence of clone 61438635

SEQ ID NO:1447 is the determined cDNA sequence of clone 61438637
SEQ ID NO:1448 is the determined cDNA sequence of clone 61438638
SEQ ID NO:1449 is the determined cDNA sequence of clone 61438639
SEQ ID NO:1450 is the determined cDNA sequence of clone 61438640
5 SEQ ID NO:1451 is the determined cDNA sequence of clone 61438641
SEQ ID NO:1452 is the determined cDNA sequence of clone 61438642
SEQ ID NO:1453 is the determined cDNA sequence of clone 61438643
SEQ ID NO:1454 is the determined cDNA sequence of clone 61438644
SEQ ID NO:1455 is the determined cDNA sequence of clone 61438645
10 SEQ ID NO:1456 is the determined cDNA sequence of clone 61438646
SEQ ID NO:1457 is the determined cDNA sequence of clone 61438647
SEQ ID NO:1458 is the determined cDNA sequence of clone 61438648
SEQ ID NO:1459 is the determined cDNA sequence of clone 61438649
SEQ ID NO:1460 is the determined cDNA sequence of clone 61438650
15 SEQ ID NO:1461 is the determined cDNA sequence of clone 61438651
SEQ ID NO:1462 is the determined cDNA sequence of clone 61438652
SEQ ID NO:1463 is the determined cDNA sequence of clone 61438653
SEQ ID NO:1464 is the determined cDNA sequence of clone 61438654
SEQ ID NO:1465 is the determined cDNA sequence of clone 61438655
20 SEQ ID NO:1466 is the determined cDNA sequence of clone 61438656
SEQ ID NO:1467 is the determined cDNA sequence of clone 61438657
SEQ ID NO:1468 is the determined cDNA sequence of clone 61438658
SEQ ID NO:1469 is the determined cDNA sequence of clone 61438659
SEQ ID NO:1470 is the determined cDNA sequence of clone 61438660
25 SEQ ID NO:1471 is the determined cDNA sequence of clone 61438661
SEQ ID NO:1472 is the determined cDNA sequence of clone 61438662
SEQ ID NO:1473 is the determined cDNA sequence of clone 61438663
SEQ ID NO:1474 is the determined cDNA sequence of clone 61438664
SEQ ID NO:1475 is the determined cDNA sequence of clone 61438665
30 SEQ ID NO:1476 is the determined cDNA sequence of clone 61165980
SEQ ID NO:1477 is the determined cDNA sequence of clone 61165981

SEQ ID NO:1478 is the determined cDNA sequence of clone 61165982
SEQ ID NO:1479 is the determined cDNA sequence of clone 61165983
SEQ ID NO:1480 is the determined cDNA sequence of clone 61165984
SEQ ID NO:1481 is the determined cDNA sequence of clone 61165985
5 SEQ ID NO:1482 is the determined cDNA sequence of clone 61165986
SEQ ID NO:1483 is the determined cDNA sequence of clone 61165987
SEQ ID NO:1484 is the determined cDNA sequence of clone 61165988
SEQ ID NO:1485 is the determined cDNA sequence of clone 61165989
SEQ ID NO:1486 is the determined cDNA sequence of clone 61165990
10 SEQ ID NO:1487 is the determined cDNA sequence of clone 61165991
SEQ ID NO:1488 is the determined cDNA sequence of clone 61165992
SEQ ID NO:1489 is the determined cDNA sequence of clone 61165994
SEQ ID NO:1490 is the determined cDNA sequence of clone 61165995
SEQ ID NO:1491 is the determined cDNA sequence of clone 61165996
15 SEQ ID NO:1492 is the determined cDNA sequence of clone 61165997
SEQ ID NO:1493 is the determined cDNA sequence of clone 61165998
SEQ ID NO:1494 is the determined cDNA sequence of clone 61165999
SEQ ID NO:1495 is the determined cDNA sequence of clone 61166001
SEQ ID NO:1496 is the determined cDNA sequence of clone 61166002
20 SEQ ID NO:1497 is the determined cDNA sequence of clone 61166003
SEQ ID NO:1498 is the determined cDNA sequence of clone 61166004
SEQ ID NO:1499 is the determined cDNA sequence of clone 61166005
SEQ ID NO:1500 is the determined cDNA sequence of clone 61166006
SEQ ID NO:1501 is the determined cDNA sequence of clone 61166007
25 SEQ ID NO:1502 is the determined cDNA sequence of clone 61166008
SEQ ID NO:1503 is the determined cDNA sequence of clone 61166009
SEQ ID NO:1504 is the determined cDNA sequence of clone 61166010
SEQ ID NO:1505 is the determined cDNA sequence of clone 61166012
SEQ ID NO:1506 is the determined cDNA sequence of clone 61166014
30 SEQ ID NO:1507 is the determined cDNA sequence of clone 61166015
SEQ ID NO:1508 is the determined cDNA sequence of clone 61166016

SEQ ID NO:1509 is the determined cDNA sequence of clone 61166017
SEQ ID NO:1510 is the determined cDNA sequence of clone 61166018
SEQ ID NO:1511 is the determined cDNA sequence of clone 61166019
SEQ ID NO:1512 is the determined cDNA sequence of clone 61166020
5 SEQ ID NO:1513 is the determined cDNA sequence of clone 61166021
SEQ ID NO:1514 is the determined cDNA sequence of clone 61166022
SEQ ID NO:1515 is the determined cDNA sequence of clone 61166023
SEQ ID NO:1516 is the determined cDNA sequence of clone 61166024
SEQ ID NO:1517 is the determined cDNA sequence of clone 61166025
10 SEQ ID NO:1518 is the determined cDNA sequence of clone 61166027
SEQ ID NO:1519 is the determined cDNA sequence of clone 61166028
SEQ ID NO:1520 is the determined cDNA sequence of clone 61166029
SEQ ID NO:1521 is the determined cDNA sequence of clone 61166030
SEQ ID NO:1522 is the determined cDNA sequence of clone 61166031
15 SEQ ID NO:1523 is the determined cDNA sequence of clone 61166032
SEQ ID NO:1524 is the determined cDNA sequence of clone 61166033
SEQ ID NO:1525 is the determined cDNA sequence of clone 61166035
SEQ ID NO:1526 is the determined cDNA sequence of clone 61166036
SEQ ID NO:1527 is the determined cDNA sequence of clone 61166039
20 SEQ ID NO:1528 is the determined cDNA sequence of clone 61166040
SEQ ID NO:1529 is the determined cDNA sequence of clone 61166041
SEQ ID NO:1530 is the determined cDNA sequence of clone 61166042
SEQ ID NO:1531 is the determined cDNA sequence of clone 61166043
SEQ ID NO:1532 is the determined cDNA sequence of clone 61166044
25 SEQ ID NO:1533 is the determined cDNA sequence of clone 61166045
SEQ ID NO:1534 is the determined cDNA sequence of clone 61166047
SEQ ID NO:1535 is the determined cDNA sequence of clone 61166048
SEQ ID NO:1536 is the determined cDNA sequence of clone 61166049
SEQ ID NO:1537 is the determined cDNA sequence of clone 61166050
30 SEQ ID NO:1538 is the determined cDNA sequence of clone 61166053
SEQ ID NO:1539 is the determined cDNA sequence of clone 61166054

SEQ ID NO:1540 is the determined cDNA sequence of clone 61166055
SEQ ID NO:1541 is the determined cDNA sequence of clone 61166056
SEQ ID NO:1542 is the determined cDNA sequence of clone 61166057
SEQ ID NO:1543 is the determined cDNA sequence of clone 61166058
5 SEQ ID NO:1544 is the determined cDNA sequence of clone 61166059
SEQ ID NO:1545 is the determined cDNA sequence of clone 61166060
SEQ ID NO:1546 is the determined cDNA sequence of clone 61166061
SEQ ID NO:1547 is the determined cDNA sequence of clone 61166062
SEQ ID NO:1548 is the determined cDNA sequence of clone 61166064
10 SEQ ID NO:1549 is the determined cDNA sequence of clone 61166065
SEQ ID NO:1550 is the determined cDNA sequence of clone 61166066
SEQ ID NO:1551 is the determined cDNA sequence of clone 61166067
SEQ ID NO:1552 is the determined cDNA sequence of clone 61166068
SEQ ID NO:1553 is the determined cDNA sequence of clone 61166069
15 SEQ ID NO:1554 is the determined cDNA sequence of clone 61166071
SEQ ID NO:1555 is the determined cDNA sequence of clone 61559232
SEQ ID NO:1556 is the determined cDNA sequence of clone 61559233
SEQ ID NO:1557 is the determined cDNA sequence of clone 61559234
SEQ ID NO:1558 is the determined cDNA sequence of clone 61559235
20 SEQ ID NO:1559 is the determined cDNA sequence of clone 61559236
SEQ ID NO:1560 is the determined cDNA sequence of clone 61559237
SEQ ID NO:1561 is the determined cDNA sequence of clone 61559238
SEQ ID NO:1562 is the determined cDNA sequence of clone 61559239
SEQ ID NO:1563 is the determined cDNA sequence of clone 61559240
25 SEQ ID NO:1564 is the determined cDNA sequence of clone 61559241
SEQ ID NO:1565 is the determined cDNA sequence of clone 61559242
SEQ ID NO:1566 is the determined cDNA sequence of clone 61559243
SEQ ID NO:1567 is the determined cDNA sequence of clone 61559244
SEQ ID NO:1568 is the determined cDNA sequence of clone 61559246
30 SEQ ID NO:1569 is the determined cDNA sequence of clone 61559247
SEQ ID NO:1570 is the determined cDNA sequence of clone 61559248

SEQ ID NO:1571 is the determined cDNA sequence of clone 61559249
SEQ ID NO:1572 is the determined cDNA sequence of clone 61559250
SEQ ID NO:1573 is the determined cDNA sequence of clone 61559251
SEQ ID NO:1574 is the determined cDNA sequence of clone 61559254
5 SEQ ID NO:1575 is the determined cDNA sequence of clone 61559255
SEQ ID NO:1576 is the determined cDNA sequence of clone 61559256
SEQ ID NO:1577 is the determined cDNA sequence of clone 61559257
SEQ ID NO:1578 is the determined cDNA sequence of clone 61559258
SEQ ID NO:1579 is the determined cDNA sequence of clone 61559259
10 SEQ ID NO:1580 is the determined cDNA sequence of clone 61559260
SEQ ID NO:1581 is the determined cDNA sequence of clone 61559261
SEQ ID NO:1582 is the determined cDNA sequence of clone 61559262
SEQ ID NO:1583 is the determined cDNA sequence of clone 61559263
SEQ ID NO:1584 is the determined cDNA sequence of clone 61559264
15 SEQ ID NO:1585 is the determined cDNA sequence of clone 61559265
SEQ ID NO:1586 is the determined cDNA sequence of clone 61559266
SEQ ID NO:1587 is the determined cDNA sequence of clone 61559267
SEQ ID NO:1588 is the determined cDNA sequence of clone 61559268
SEQ ID NO:1589 is the determined cDNA sequence of clone 61559270
20 SEQ ID NO:1590 is the determined cDNA sequence of clone 61559271
SEQ ID NO:1591 is the determined cDNA sequence of clone 61559272
SEQ ID NO:1592 is the determined cDNA sequence of clone 61559273
SEQ ID NO:1593 is the determined cDNA sequence of clone 61559274
SEQ ID NO:1594 is the determined cDNA sequence of clone 61559275
25 SEQ ID NO:1595 is the determined cDNA sequence of clone 61559276
SEQ ID NO:1596 is the determined cDNA sequence of clone 61559277
SEQ ID NO:1597 is the determined cDNA sequence of clone 61559278
SEQ ID NO:1598 is the determined cDNA sequence of clone 61559279
SEQ ID NO:1599 is the determined cDNA sequence of clone 61559280
30 SEQ ID NO:1600 is the determined cDNA sequence of clone 61559281
SEQ ID NO:1601 is the determined cDNA sequence of clone 61559282

SEQ ID NO:1602 is the determined cDNA sequence of clone 61559283
SEQ ID NO:1603 is the determined cDNA sequence of clone 61559284
SEQ ID NO:1604 is the determined cDNA sequence of clone 61559285
SEQ ID NO:1605 is the determined cDNA sequence of clone 61559286
5 SEQ ID NO:1606 is the determined cDNA sequence of clone 61559287
SEQ ID NO:1607 is the determined cDNA sequence of clone 61559288
SEQ ID NO:1608 is the determined cDNA sequence of clone 61559289
SEQ ID NO:1609 is the determined cDNA sequence of clone 61559290
SEQ ID NO:1610 is the determined cDNA sequence of clone 61559291
10 SEQ ID NO:1611 is the determined cDNA sequence of clone 61559292
SEQ ID NO:1612 is the determined cDNA sequence of clone 61559293
SEQ ID NO:1613 is the determined cDNA sequence of clone 61559294
SEQ ID NO:1614 is the determined cDNA sequence of clone 61559295
SEQ ID NO:1615 is the determined cDNA sequence of clone 61559296
15 SEQ ID NO:1616 is the determined cDNA sequence of clone 61559297
SEQ ID NO:1617 is the determined cDNA sequence of clone 61559298
SEQ ID NO:1618 is the determined cDNA sequence of clone 61559299
SEQ ID NO:1619 is the determined cDNA sequence of clone 61559300
SEQ ID NO:1620 is the determined cDNA sequence of clone 61559302
20 SEQ ID NO:1621 is the determined cDNA sequence of clone 61559303
SEQ ID NO:1622 is the determined cDNA sequence of clone 61559304
SEQ ID NO:1623 is the determined cDNA sequence of clone 61559305
SEQ ID NO:1624 is the determined cDNA sequence of clone 61559306
SEQ ID NO:1625 is the determined cDNA sequence of clone 61559308
25 SEQ ID NO:1626 is the determined cDNA sequence of clone 61559310
SEQ ID NO:1627 is the determined cDNA sequence of clone 61559311
SEQ ID NO:1628 is the determined cDNA sequence of clone 61559312
SEQ ID NO:1629 is the determined cDNA sequence of clone 61559313
SEQ ID NO:1630 is the determined cDNA sequence of clone 61559314
30 SEQ ID NO:1631 is the determined cDNA sequence of clone 61559315
SEQ ID NO:1632 is the determined cDNA sequence of clone 61559316

SEQ ID NO:1633 is the determined cDNA sequence of clone 61559318
SEQ ID NO:1634 is the determined cDNA sequence of clone 61559319
SEQ ID NO:1635 is the determined cDNA sequence of clone 61559320
SEQ ID NO:1636 is the determined cDNA sequence of clone 61559321
5 SEQ ID NO:1637 is the determined cDNA sequence of clone 61559322
SEQ ID NO:1638 is the determined cDNA sequence of clone 61559324
SEQ ID NO:1639 is the determined cDNA sequence of clone 61438387
SEQ ID NO:1640 is the determined cDNA sequence of clone 61438388
SEQ ID NO:1641 is the determined cDNA sequence of clone 61438390
10 SEQ ID NO:1642 is the determined cDNA sequence of clone 61438391
SEQ ID NO:1643 is the determined cDNA sequence of clone 61438394
SEQ ID NO:1644 is the determined cDNA sequence of clone 61438397
SEQ ID NO:1645 is the determined cDNA sequence of clone 61438398
SEQ ID NO:1646 is the determined cDNA sequence of clone 61438399
15 SEQ ID NO:1647 is the determined cDNA sequence of clone 61438400
SEQ ID NO:1648 is the determined cDNA sequence of clone 61438401
SEQ ID NO:1649 is the determined cDNA sequence of clone 61438403
SEQ ID NO:1650 is the determined cDNA sequence of clone 61438404
SEQ ID NO:1651 is the determined cDNA sequence of clone 61438405
20 SEQ ID NO:1652 is the determined cDNA sequence of clone 61438406
SEQ ID NO:1653 is the determined cDNA sequence of clone 61438407
SEQ ID NO:1654 is the determined cDNA sequence of clone 61438408
SEQ ID NO:1655 is the determined cDNA sequence of clone 61438409
SEQ ID NO:1656 is the determined cDNA sequence of clone 61438410
25 SEQ ID NO:1657 is the determined cDNA sequence of clone 61438411
SEQ ID NO:1658 is the determined cDNA sequence of clone 61438412
SEQ ID NO:1659 is the determined cDNA sequence of clone 61438414
SEQ ID NO:1660 is the determined cDNA sequence of clone 61438415
SEQ ID NO:1661 is the determined cDNA sequence of clone 61438416
30 SEQ ID NO:1662 is the determined cDNA sequence of clone 61438417
SEQ ID NO:1663 is the determined cDNA sequence of clone 61438418

SEQ ID NO:1664 is the determined cDNA sequence of clone 61438419
SEQ ID NO:1665 is the determined cDNA sequence of clone 61438420
SEQ ID NO:1666 is the determined cDNA sequence of clone 61438421
SEQ ID NO:1667 is the determined cDNA sequence of clone 61438422
5 SEQ ID NO:1668 is the determined cDNA sequence of clone 61438423
SEQ ID NO:1669 is the determined cDNA sequence of clone 61438424
SEQ ID NO:1670 is the determined cDNA sequence of clone 61438425
SEQ ID NO:1671 is the determined cDNA sequence of clone 61438426
SEQ ID NO:1672 is the determined cDNA sequence of clone 61438427
10 SEQ ID NO:1673 is the determined cDNA sequence of clone 61438428
SEQ ID NO:1674 is the determined cDNA sequence of clone 61438429
SEQ ID NO:1675 is the determined cDNA sequence of clone 61438430
SEQ ID NO:1676 is the determined cDNA sequence of clone 61438431
SEQ ID NO:1677 is the determined cDNA sequence of clone 61438432
15 SEQ ID NO:1678 is the determined cDNA sequence of clone 61438435
SEQ ID NO:1679 is the determined cDNA sequence of clone 61438436
SEQ ID NO:1680 is the determined cDNA sequence of clone 61438437
SEQ ID NO:1681 is the determined cDNA sequence of clone 61438438
SEQ ID NO:1682 is the determined cDNA sequence of clone 61438439
20 SEQ ID NO:1683 is the determined cDNA sequence of clone 61438440
SEQ ID NO:1684 is the determined cDNA sequence of clone 61438441
SEQ ID NO:1685 is the determined cDNA sequence of clone 61438442
SEQ ID NO:1686 is the determined cDNA sequence of clone 61438443
SEQ ID NO:1687 is the determined cDNA sequence of clone 61438444
25 SEQ ID NO:1688 is the determined cDNA sequence of clone 61438446
SEQ ID NO:1689 is the determined cDNA sequence of clone 61438448
SEQ ID NO:1690 is the determined cDNA sequence of clone 61438449
SEQ ID NO:1691 is the determined cDNA sequence of clone 61438450
SEQ ID NO:1692 is the determined cDNA sequence of clone 61438451
30 SEQ ID NO:1693 is the determined cDNA sequence of clone 61438452
SEQ ID NO:1694 is the determined cDNA sequence of clone 61438453

SEQ ID NO:1695 is the determined cDNA sequence of clone 61438454
SEQ ID NO:1696 is the determined cDNA sequence of clone 61438455
SEQ ID NO:1697 is the determined cDNA sequence of clone 61438456
SEQ ID NO:1698 is the determined cDNA sequence of clone 61438458
5 SEQ ID NO:1699 is the determined cDNA sequence of clone 61438459
SEQ ID NO:1700 is the determined cDNA sequence of clone 61438463
SEQ ID NO:1701 is the determined cDNA sequence of clone 61438465
SEQ ID NO:1702 is the determined cDNA sequence of clone 61438466
SEQ ID NO:1703 is the determined cDNA sequence of clone 61438467
10 SEQ ID NO:1704 is the determined cDNA sequence of clone 61438468
SEQ ID NO:1705 is the determined cDNA sequence of clone 61438469
SEQ ID NO:1706 is the determined cDNA sequence of clone 61438470
SEQ ID NO:1707 is the determined cDNA sequence of clone 61438471
SEQ ID NO:1708 is the determined cDNA sequence of clone 61438472
15 SEQ ID NO:1709 is the determined cDNA sequence of clone 61438474
SEQ ID NO:1710 is the determined cDNA sequence of clone 61438475
SEQ ID NO:1711 is the determined cDNA sequence of clone 61438476
SEQ ID NO:1712 is the determined cDNA sequence of clone 61438478
SEQ ID NO:1713 is the determined cDNA sequence of clone 61438479
20 SEQ ID NO:1714 is the determined cDNA sequence of clone 61524872
SEQ ID NO:1715 is the determined cDNA sequence of clone 61524873
SEQ ID NO:1716 is the determined cDNA sequence of clone 61524874
SEQ ID NO:1717 is the determined cDNA sequence of clone 61524876
SEQ ID NO:1718 is the determined cDNA sequence of clone 61524877
25 SEQ ID NO:1719 is the determined cDNA sequence of clone 61524878
SEQ ID NO:1720 is the determined cDNA sequence of clone 61524879
SEQ ID NO:1721 is the determined cDNA sequence of clone 61524880
SEQ ID NO:1722 is the determined cDNA sequence of clone 61524881
SEQ ID NO:1723 is the determined cDNA sequence of clone 61524882
30 SEQ ID NO:1724 is the determined cDNA sequence of clone 61524883
SEQ ID NO:1725 is the determined cDNA sequence of clone 61524884

SEQ ID NO:1726 is the determined cDNA sequence of clone 61524886
SEQ ID NO:1727 is the determined cDNA sequence of clone 61524887
SEQ ID NO:1728 is the determined cDNA sequence of clone 61524888
SEQ ID NO:1729 is the determined cDNA sequence of clone 61524889
5 SEQ ID NO:1730 is the determined cDNA sequence of clone 61524890
SEQ ID NO:1731 is the determined cDNA sequence of clone 61524891
SEQ ID NO:1732 is the determined cDNA sequence of clone 61524892
SEQ ID NO:1733 is the determined cDNA sequence of clone 61524893
SEQ ID NO:1734 is the determined cDNA sequence of clone 61524894
10 SEQ ID NO:1735 is the determined cDNA sequence of clone 61524895
SEQ ID NO:1736 is the determined cDNA sequence of clone 61524897
SEQ ID NO:1737 is the determined cDNA sequence of clone 61524898
SEQ ID NO:1738 is the determined cDNA sequence of clone 61524899
SEQ ID NO:1739 is the determined cDNA sequence of clone 61524901
15 SEQ ID NO:1740 is the determined cDNA sequence of clone 61524902
SEQ ID NO:1741 is the determined cDNA sequence of clone 61524903
SEQ ID NO:1742 is the determined cDNA sequence of clone 61524904
SEQ ID NO:1743 is the determined cDNA sequence of clone 61524905
SEQ ID NO:1744 is the determined cDNA sequence of clone 61524906
20 SEQ ID NO:1745 is the determined cDNA sequence of clone 61524908
SEQ ID NO:1746 is the determined cDNA sequence of clone 61524909
SEQ ID NO:1747 is the determined cDNA sequence of clone 61524910
SEQ ID NO:1748 is the determined cDNA sequence of clone 61524912
SEQ ID NO:1749 is the determined cDNA sequence of clone 61524913
25 SEQ ID NO:1750 is the determined cDNA sequence of clone 61524914
SEQ ID NO:1751 is the determined cDNA sequence of clone 61524915
SEQ ID NO:1752 is the determined cDNA sequence of clone 61524916
SEQ ID NO:1753 is the determined cDNA sequence of clone 61524918
SEQ ID NO:1754 is the determined cDNA sequence of clone 61524919
30 SEQ ID NO:1755 is the determined cDNA sequence of clone 61524920
SEQ ID NO:1756 is the determined cDNA sequence of clone 61524923

SEQ ID NO:1757 is the determined cDNA sequence of clone 61524924
SEQ ID NO:1758 is the determined cDNA sequence of clone 61524925
SEQ ID NO:1759 is the determined cDNA sequence of clone 61524926
SEQ ID NO:1760 is the determined cDNA sequence of clone 61524927
5 SEQ ID NO:1761 is the determined cDNA sequence of clone 61524933
SEQ ID NO:1762 is the determined cDNA sequence of clone 61524935
SEQ ID NO:1763 is the determined cDNA sequence of clone 61524937
SEQ ID NO:1764 is the determined cDNA sequence of clone 61524939
SEQ ID NO:1765 is the determined cDNA sequence of clone 61524941
10 SEQ ID NO:1766 is the determined cDNA sequence of clone 61524942
SEQ ID NO:1767 is the determined cDNA sequence of clone 61524943
SEQ ID NO:1768 is the determined cDNA sequence of clone 61524944
SEQ ID NO:1769 is the determined cDNA sequence of clone 61524945
SEQ ID NO:1770 is the determined cDNA sequence of clone 61524946
15 SEQ ID NO:1771 is the determined cDNA sequence of clone 61524947
SEQ ID NO:1772 is the determined cDNA sequence of clone 61524948
SEQ ID NO:1773 is the determined cDNA sequence of clone 61524949
SEQ ID NO:1774 is the determined cDNA sequence of clone 61524950
SEQ ID NO:1775 is the determined cDNA sequence of clone 61524952
20 SEQ ID NO:1776 is the determined cDNA sequence of clone 61524953
SEQ ID NO:1777 is the determined cDNA sequence of clone 61524954
SEQ ID NO:1778 is the determined cDNA sequence of clone 61524956
SEQ ID NO:1779 is the determined cDNA sequence of clone 61524957
SEQ ID NO:1780 is the determined cDNA sequence of clone 61524958
25 SEQ ID NO:1781 is the determined cDNA sequence of clone 61524961
SEQ ID NO:1782 is the determined cDNA sequence of clone 61524962
SEQ ID NO:1783 is the determined cDNA sequence of clone 61524963
SEQ ID NO:1784 is the determined cDNA sequence of clone 61524964
SEQ ID NO:1785 is the determined cDNA sequence of clone 61547629
30 SEQ ID NO:1786 is the determined cDNA sequence of clone 61547630
SEQ ID NO:1787 is the determined cDNA sequence of clone 61547631

SEQ ID NO:1788 is the determined cDNA sequence of clone 61547632
SEQ ID NO:1789 is the determined cDNA sequence of clone 61547634
SEQ ID NO:1790 is the determined cDNA sequence of clone 61547635
SEQ ID NO:1791 is the determined cDNA sequence of clone 61547636
5 SEQ ID NO:1792 is the determined cDNA sequence of clone 61547637
SEQ ID NO:1793 is the determined cDNA sequence of clone 61547638
SEQ ID NO:1794 is the determined cDNA sequence of clone 61547639
SEQ ID NO:1795 is the determined cDNA sequence of clone 61547640
SEQ ID NO:1796 is the determined cDNA sequence of clone 61547644
10 SEQ ID NO:1797 is the determined cDNA sequence of clone 61547646
SEQ ID NO:1798 is the determined cDNA sequence of clone 61547647
SEQ ID NO:1799 is the determined cDNA sequence of clone 61547648
SEQ ID NO:1800 is the determined cDNA sequence of clone 61547652
SEQ ID NO:1801 is the determined cDNA sequence of clone 61547653
15 SEQ ID NO:1802 is the determined cDNA sequence of clone 61547654
SEQ ID NO:1803 is the determined cDNA sequence of clone 61547656
SEQ ID NO:1804 is the determined cDNA sequence of clone 61547657
SEQ ID NO:1805 is the determined cDNA sequence of clone 61547658
SEQ ID NO:1806 is the determined cDNA sequence of clone 61547659
20 SEQ ID NO:1807 is the determined cDNA sequence of clone 61547660
SEQ ID NO:1808 is the determined cDNA sequence of clone 61547661
SEQ ID NO:1809 is the determined cDNA sequence of clone 61547662
SEQ ID NO:1810 is the determined cDNA sequence of clone 61547664
SEQ ID NO:1811 is the determined cDNA sequence of clone 61547665
25 SEQ ID NO:1812 is the determined cDNA sequence of clone 61547666
SEQ ID NO:1813 is the determined cDNA sequence of clone 61547667
SEQ ID NO:1814 is the determined cDNA sequence of clone 61547669
SEQ ID NO:1815 is the determined cDNA sequence of clone 61547670
SEQ ID NO:1816 is the determined cDNA sequence of clone 61547671
30 SEQ ID NO:1817 is the determined cDNA sequence of clone 61547672
SEQ ID NO:1818 is the determined cDNA sequence of clone 61547673

SEQ ID NO:1819 is the determined cDNA sequence of clone 61547674
SEQ ID NO:1820 is the determined cDNA sequence of clone 61547675
SEQ ID NO:1821 is the determined cDNA sequence of clone 61547678
SEQ ID NO:1822 is the determined cDNA sequence of clone 61547679
5 SEQ ID NO:1823 is the determined cDNA sequence of clone 61547680
SEQ ID NO:1824 is the determined cDNA sequence of clone 61547681
SEQ ID NO:1825 is the determined cDNA sequence of clone 61547682
SEQ ID NO:1826 is the determined cDNA sequence of clone 61547683
SEQ ID NO:1827 is the determined cDNA sequence of clone 61547685
10 SEQ ID NO:1828 is the determined cDNA sequence of clone 61547686
SEQ ID NO:1829 is the determined cDNA sequence of clone 61547687
SEQ ID NO:1830 is the determined cDNA sequence of clone 61547689
SEQ ID NO:1831 is the determined cDNA sequence of clone 61547690
SEQ ID NO:1832 is the determined cDNA sequence of clone 61547691
15 SEQ ID NO:1833 is the determined cDNA sequence of clone 61547692
SEQ ID NO:1834 is the determined cDNA sequence of clone 61547695
SEQ ID NO:1835 is the determined cDNA sequence of clone 61547696
SEQ ID NO:1836 is the determined cDNA sequence of clone 61547697
SEQ ID NO:1837 is the determined cDNA sequence of clone 61547698
20 SEQ ID NO:1838 is the determined cDNA sequence of clone 61547699
SEQ ID NO:1839 is the determined cDNA sequence of clone 61547700
SEQ ID NO:1840 is the determined cDNA sequence of clone 61547701
SEQ ID NO:1841 is the determined cDNA sequence of clone 61547702
SEQ ID NO:1842 is the determined cDNA sequence of clone 61547703
25 SEQ ID NO:1843 is the determined cDNA sequence of clone 61547704
SEQ ID NO:1844 is the determined cDNA sequence of clone 61547705
SEQ ID NO:1845 is the determined cDNA sequence of clone 61547706
SEQ ID NO:1846 is the determined cDNA sequence of clone 61547707
SEQ ID NO:1847 is the determined cDNA sequence of clone 61547708
30 SEQ ID NO:1848 is the determined cDNA sequence of clone 61547710
SEQ ID NO:1849 is the determined cDNA sequence of clone 61547711

SEQ ID NO:1850 is the determined cDNA sequence of clone 61547712
SEQ ID NO:1851 is the determined cDNA sequence of clone 61547713
SEQ ID NO:1852 is the determined cDNA sequence of clone 61547714
SEQ ID NO:1853 is the determined cDNA sequence of clone 61547716
5 SEQ ID NO:1854 is the determined cDNA sequence of clone 61547718
SEQ ID NO:1855 is the determined cDNA sequence of clone 61547720
SEQ ID NO:1856 is the determined cDNA sequence of clone 61547722
SEQ ID NO:1857 is the determined cDNA sequence of clone 61547724
SEQ ID NO:1858 is the determined cDNA sequence of clone 61547725
10 SEQ ID NO:1859 is the determined cDNA sequence of clone 61547727
SEQ ID NO:1860 is the determined cDNA sequence of clone 61547728
SEQ ID NO:1861 is the determined cDNA sequence of clone 61547729
SEQ ID NO:1862 is the determined cDNA sequence of clone 61547730
SEQ ID NO:1863 is the determined cDNA sequence of clone 61547731
15 SEQ ID NO:1864 is the determined cDNA sequence of clone 61547733
SEQ ID NO:1865 is the determined cDNA sequence of clone 61547734
SEQ ID NO:1866 is the determined cDNA sequence of clone 61547735
SEQ ID NO:1867 is the determined cDNA sequence of clone 61547736
SEQ ID NO:1868 is the determined cDNA sequence of clone 61547737
20 SEQ ID NO:1869 is the determined cDNA sequence of clone 61547738
SEQ ID NO:1870 is the determined cDNA sequence of clone 61547739
SEQ ID NO:1871 is the determined cDNA sequence of clone 61547740
SEQ ID NO:1872 is the determined cDNA sequence of clone 61547741
SEQ ID NO:1873 is the determined cDNA sequence of clone 61547742
25 SEQ ID NO:1874 is the determined cDNA sequence of clone 61547743
SEQ ID NO:1875 is the determined cDNA sequence of clone 61547745
SEQ ID NO:1876 is the determined cDNA sequence of clone 61547746
SEQ ID NO:1877 is the determined cDNA sequence of clone 61547747
SEQ ID NO:1878 is the determined cDNA sequence of clone 61547748
30 SEQ ID NO:1879 is the determined cDNA sequence of clone 61547749
SEQ ID NO:1880 is the determined cDNA sequence of clone 61547750

SEQ ID NO:1881 is the determined cDNA sequence of clone 61547753
SEQ ID NO:1882 is the determined cDNA sequence of clone 61547754
SEQ ID NO:1883 is the determined cDNA sequence of clone 61547755
SEQ ID NO:1884 is the determined cDNA sequence of clone 61547756
5 SEQ ID NO:1885 is the determined cDNA sequence of clone 61547757
SEQ ID NO:1886 is the determined cDNA sequence of clone 61547759
SEQ ID NO:1887 is the determined cDNA sequence of clone 61547760
SEQ ID NO:1888 is the determined cDNA sequence of clone 61547761
SEQ ID NO:1889 is the determined cDNA sequence of clone 61547763
10 SEQ ID NO:1890 is the determined cDNA sequence of clone 61547764
SEQ ID NO:1891 is the determined cDNA sequence of clone 61547765
SEQ ID NO:1892 is the determined cDNA sequence of clone 61547766
SEQ ID NO:1893 is the determined cDNA sequence of clone 61547767
SEQ ID NO:1894 is the determined cDNA sequence of clone 61547769
15 SEQ ID NO:1895 is the determined cDNA sequence of clone 61547774
SEQ ID NO:1896 is the determined cDNA sequence of clone 61547775
SEQ ID NO:1897 is the determined cDNA sequence of clone 61547776
SEQ ID NO:1898 is the determined cDNA sequence of clone 61547777
SEQ ID NO:1899 is the determined cDNA sequence of clone 61547778
20 SEQ ID NO:1900 is the determined cDNA sequence of clone 61547779
SEQ ID NO:1901 is the determined cDNA sequence of clone 61547782
SEQ ID NO:1902 is the determined cDNA sequence of clone 61547783
SEQ ID NO:1903 is the determined cDNA sequence of clone 61547785
SEQ ID NO:1904 is the determined cDNA sequence of clone 61547786
25 SEQ ID NO:1905 is the determined cDNA sequence of clone 61547787
SEQ ID NO:1906 is the determined cDNA sequence of clone 61547788
SEQ ID NO:1907 is the determined cDNA sequence of clone 61547789
SEQ ID NO:1908 is the determined cDNA sequence of clone 61547790
SEQ ID NO:1909 is the determined cDNA sequence of clone 61547791
30 SEQ ID NO:1910 is the determined cDNA sequence of clone 61547792
SEQ ID NO:1911 is the determined cDNA sequence of clone 61547793

SEQ ID NO:1912 is the determined cDNA sequence of clone 61547795
SEQ ID NO:1913 is the determined cDNA sequence of clone 61547796
SEQ ID NO:1914 is the determined cDNA sequence of clone 61547797
SEQ ID NO:1915 is the determined cDNA sequence of clone 61547800
5 SEQ ID NO:1916 is the determined cDNA sequence of clone 61547801
SEQ ID NO:1917 is the determined cDNA sequence of clone 61547804
SEQ ID NO:1918 is the determined cDNA sequence of clone 61547805
SEQ ID NO:1919 is the determined cDNA sequence of clone 61547806
SEQ ID NO:1920 is the determined cDNA sequence of clone 61547808
10 SEQ ID NO:1921 is the determined cDNA sequence of clone 61547809
SEQ ID NO:1922 is the determined cDNA sequence of clone 61547810
SEQ ID NO:1923 is the determined cDNA sequence of clone 61547811
SEQ ID NO:1924 is the determined cDNA sequence of clone 61547812
SEQ ID NO:1925 is the determined cDNA sequence of clone 61547813
15 SEQ ID NO:1926 is the determined cDNA sequence of clone 61547814
SEQ ID NO:1927 is the determined cDNA sequence of clone 61496272
SEQ ID NO:1928 is the determined cDNA sequence of clone 61496273
SEQ ID NO:1929 is the determined cDNA sequence of clone 61496274
SEQ ID NO:1930 is the determined cDNA sequence of clone 61496275
20 SEQ ID NO:1931 is the determined cDNA sequence of clone 61496276
SEQ ID NO:1932 is the determined cDNA sequence of clone 61496277
SEQ ID NO:1933 is the determined cDNA sequence of clone 61496278
SEQ ID NO:1934 is the determined cDNA sequence of clone 61496279
SEQ ID NO:1935 is the determined cDNA sequence of clone 61496280
25 SEQ ID NO:1936 is the determined cDNA sequence of clone 61496281
SEQ ID NO:1937 is the determined cDNA sequence of clone 61496282
SEQ ID NO:1938 is the determined cDNA sequence of clone 61496283
SEQ ID NO:1939 is the determined cDNA sequence of clone 61496285
SEQ ID NO:1940 is the determined cDNA sequence of clone 61496286
30 SEQ ID NO:1941 is the determined cDNA sequence of clone 61496287
SEQ ID NO:1942 is the determined cDNA sequence of clone 61496288

SEQ ID NO:1943 is the determined cDNA sequence of clone 61496289
SEQ ID NO:1944 is the determined cDNA sequence of clone 61496290
SEQ ID NO:1945 is the determined cDNA sequence of clone 61496291
SEQ ID NO:1946 is the determined cDNA sequence of clone 61496292
5 SEQ ID NO:1947 is the determined cDNA sequence of clone 61496293
SEQ ID NO:1948 is the determined cDNA sequence of clone 61496294
SEQ ID NO:1949 is the determined cDNA sequence of clone 61496295
SEQ ID NO:1950 is the determined cDNA sequence of clone 61496298
SEQ ID NO:1951 is the determined cDNA sequence of clone 61496299
10 SEQ ID NO:1952 is the determined cDNA sequence of clone 61496300
SEQ ID NO:1953 is the determined cDNA sequence of clone 61496301
SEQ ID NO:1954 is the determined cDNA sequence of clone 61496302
SEQ ID NO:1955 is the determined cDNA sequence of clone 61496303
SEQ ID NO:1956 is the determined cDNA sequence of clone 61496304
15 SEQ ID NO:1957 is the determined cDNA sequence of clone 61496305
SEQ ID NO:1958 is the determined cDNA sequence of clone 61496308
SEQ ID NO:1959 is the determined cDNA sequence of clone 61496309
SEQ ID NO:1960 is the determined cDNA sequence of clone 61496310
SEQ ID NO:1961 is the determined cDNA sequence of clone 61496312
20 SEQ ID NO:1962 is the determined cDNA sequence of clone 61496313
SEQ ID NO:1963 is the determined cDNA sequence of clone 61496314
SEQ ID NO:1964 is the determined cDNA sequence of clone 61496315
SEQ ID NO:1965 is the determined cDNA sequence of clone 61496316
SEQ ID NO:1966 is the determined cDNA sequence of clone 61496317
25 SEQ ID NO:1967 is the determined cDNA sequence of clone 61496318
SEQ ID NO:1968 is the determined cDNA sequence of clone 61496319
SEQ ID NO:1969 is the determined cDNA sequence of clone 61496320
SEQ ID NO:1970 is the determined cDNA sequence of clone 61496322
SEQ ID NO:1971 is the determined cDNA sequence of clone 61496323
30 SEQ ID NO:1972 is the determined cDNA sequence of clone 61496324
SEQ ID NO:1973 is the determined cDNA sequence of clone 61496325

SEQ ID NO:1974 is the determined cDNA sequence of clone 61496326
SEQ ID NO:1975 is the determined cDNA sequence of clone 61496327
SEQ ID NO:1976 is the determined cDNA sequence of clone 61496328
SEQ ID NO:1977 is the determined cDNA sequence of clone 61496329
5 SEQ ID NO:1978 is the determined cDNA sequence of clone 61496330
SEQ ID NO:1979 is the determined cDNA sequence of clone 61496331
SEQ ID NO:1980 is the determined cDNA sequence of clone 61496332
SEQ ID NO:1981 is the determined cDNA sequence of clone 61496333
SEQ ID NO:1982 is the determined cDNA sequence of clone 61496334
10 SEQ ID NO:1983 is the determined cDNA sequence of clone 61496335
SEQ ID NO:1984 is the determined cDNA sequence of clone 61496336
SEQ ID NO:1985 is the determined cDNA sequence of clone 61496337
SEQ ID NO:1986 is the determined cDNA sequence of clone 61496338
SEQ ID NO:1987 is the determined cDNA sequence of clone 61496340
15 SEQ ID NO:1988 is the determined cDNA sequence of clone 61496341
SEQ ID NO:1989 is the determined cDNA sequence of clone 61496342
SEQ ID NO:1990 is the determined cDNA sequence of clone 61496343
SEQ ID NO:1991 is the determined cDNA sequence of clone 61496345
SEQ ID NO:1992 is the determined cDNA sequence of clone 61496346
20 SEQ ID NO:1993 is the determined cDNA sequence of clone 61496347
SEQ ID NO:1994 is the determined cDNA sequence of clone 61496348
SEQ ID NO:1995 is the determined cDNA sequence of clone 61496349
SEQ ID NO:1996 is the determined cDNA sequence of clone 61496351
SEQ ID NO:1997 is the determined cDNA sequence of clone 61496352
25 SEQ ID NO:1998 is the determined cDNA sequence of clone 61496353
SEQ ID NO:1999 is the determined cDNA sequence of clone 61496355
SEQ ID NO:2000 is the determined cDNA sequence of clone 61496356
SEQ ID NO:2001 is the determined cDNA sequence of clone 61496357
SEQ ID NO:2002 is the determined cDNA sequence of clone 61496358
30 SEQ ID NO:2003 is the determined cDNA sequence of clone 61496359
SEQ ID NO:2004 is the determined cDNA sequence of clone 61496360

SEQ ID NO:2005 is the determined cDNA sequence of clone 61496362
SEQ ID NO:2006 is the determined cDNA sequence of clone 61496363
SEQ ID NO:2007 is the determined cDNA sequence of clone 61496364
SEQ ID NO:2008 is the determined cDNA sequence of clone 61496373
5 SEQ ID NO:2009 is the determined cDNA sequence of clone 61496374
SEQ ID NO:2010 is the determined cDNA sequence of clone 61496375
SEQ ID NO:2011 is the determined cDNA sequence of clone 61496376
SEQ ID NO:2012 is the determined cDNA sequence of clone 61496378
SEQ ID NO:2013 is the determined cDNA sequence of clone 61496379
10 SEQ ID NO:2014 is the determined cDNA sequence of clone 61496380
SEQ ID NO:2015 is the determined cDNA sequence of clone 61496381
SEQ ID NO:2016 is the determined cDNA sequence of clone 61496383
SEQ ID NO:2017 is the determined cDNA sequence of clone 61496384
SEQ ID NO:2018 is the determined cDNA sequence of clone 61496386
15 SEQ ID NO:2019 is the determined cDNA sequence of clone 61496388
SEQ ID NO:2020 is the determined cDNA sequence of clone 61496390
SEQ ID NO:2021 is the determined cDNA sequence of clone 61496391
SEQ ID NO:2022 is the determined cDNA sequence of clone 61496394
SEQ ID NO:2023 is the determined cDNA sequence of clone 61496395
20 SEQ ID NO:2024 is the determined cDNA sequence of clone 61496398
SEQ ID NO:2025 is the determined cDNA sequence of clone 61496399
SEQ ID NO:2026 is the determined cDNA sequence of clone 61496400
SEQ ID NO:2027 is the determined cDNA sequence of clone 61496401
SEQ ID NO:2028 is the determined cDNA sequence of clone 61496402
25 SEQ ID NO:2029 is the determined cDNA sequence of clone 61496403
SEQ ID NO:2030 is the determined cDNA sequence of clone 61496404
SEQ ID NO:2031 is the determined cDNA sequence of clone 61496405
SEQ ID NO:2032 is the determined cDNA sequence of clone 61496406
SEQ ID NO:2033 is the determined cDNA sequence of clone 61496407
30 SEQ ID NO:2034 is the determined cDNA sequence of clone 61496408
SEQ ID NO:2035 is the determined cDNA sequence of clone 61496410

SEQ ID NO:2036 is the determined cDNA sequence of clone 61496411
SEQ ID NO:2037 is the determined cDNA sequence of clone 61496412
SEQ ID NO:2038 is the determined cDNA sequence of clone 61496413
SEQ ID NO:2039 is the determined cDNA sequence of clone 61496414
5 SEQ ID NO:2040 is the determined cDNA sequence of clone 61496416
SEQ ID NO:2041 is the determined cDNA sequence of clone 61496417
SEQ ID NO:2042 is the determined cDNA sequence of clone 61496418
SEQ ID NO:2043 is the determined cDNA sequence of clone 61496419
SEQ ID NO:2044 is the determined cDNA sequence of clone 61496420
10 SEQ ID NO:2045 is the determined cDNA sequence of clone 61496422
SEQ ID NO:2046 is the determined cDNA sequence of clone 61496423
SEQ ID NO:2047 is the determined cDNA sequence of clone 61496426
SEQ ID NO:2048 is the determined cDNA sequence of clone 61496427
SEQ ID NO:2049 is the determined cDNA sequence of clone 61496429
15 SEQ ID NO:2050 is the determined cDNA sequence of clone 61496430
SEQ ID NO:2051 is the determined cDNA sequence of clone 61496431
SEQ ID NO:2052 is the determined cDNA sequence of clone 61496432
SEQ ID NO:2053 is the determined cDNA sequence of clone 61496435
SEQ ID NO:2054 is the determined cDNA sequence of clone 61496436
20 SEQ ID NO:2055 is the determined cDNA sequence of clone 61496437
SEQ ID NO:2056 is the determined cDNA sequence of clone 61496438
SEQ ID NO:2057 is the determined cDNA sequence of clone 61496439
SEQ ID NO:2058 is the determined cDNA sequence of clone 61496440
SEQ ID NO:2059 is the determined cDNA sequence of clone 61496441
25 SEQ ID NO:2060 is the determined cDNA sequence of clone 61496442
SEQ ID NO:2061 is the determined cDNA sequence of clone 61496443
SEQ ID NO:2062 is the determined cDNA sequence of clone 61496444
SEQ ID NO:2063 is the determined cDNA sequence of clone 61496445
SEQ ID NO:2064 is the determined cDNA sequence of clone 61496446
30 SEQ ID NO:2065 is the determined cDNA sequence of clone 61496447
SEQ ID NO:2066 is the determined cDNA sequence of clone 61496449

SEQ ID NO:2067 is the determined cDNA sequence of clone 61496451
SEQ ID NO:2068 is the determined cDNA sequence of clone 61496452
SEQ ID NO:2069 is the determined cDNA sequence of clone 61496454
SEQ ID NO:2070 is the determined cDNA sequence of clone 61496455
5 SEQ ID NO:2071 is the determined cDNA sequence of clone 61496456
SEQ ID NO:2072 is the determined cDNA sequence of clone 61496458
SEQ ID NO:2073 is the determined cDNA sequence of clone 61496459
SEQ ID NO:2074 is the determined cDNA sequence of clone 61496461
SEQ ID NO:2075 is the determined cDNA sequence of clone 61496463
10 SEQ ID NO:2076 is the determined cDNA sequence of clone 61496464
SEQ ID NO:2077 is the determined cDNA sequence of clone 61496465
SEQ ID NO:2078 is the determined cDNA sequence of clone 61438480
SEQ ID NO:2079 is the determined cDNA sequence of clone 61438482
SEQ ID NO:2080 is the determined cDNA sequence of clone 61438484
15 SEQ ID NO:2081 is the determined cDNA sequence of clone 61438485
SEQ ID NO:2082 is the determined cDNA sequence of clone 61438486
SEQ ID NO:2083 is the determined cDNA sequence of clone 61438488
SEQ ID NO:2084 is the determined cDNA sequence of clone 61438489
SEQ ID NO:2085 is the determined cDNA sequence of clone 61438492
20 SEQ ID NO:2086 is the determined cDNA sequence of clone 61438493
SEQ ID NO:2087 is the determined cDNA sequence of clone 61438495
SEQ ID NO:2088 is the determined cDNA sequence of clone 61438496
SEQ ID NO:2089 is the determined cDNA sequence of clone 61438497
SEQ ID NO:2090 is the determined cDNA sequence of clone 61438500
25 SEQ ID NO:2091 is the determined cDNA sequence of clone 61438501
SEQ ID NO:2092 is the determined cDNA sequence of clone 61438503
SEQ ID NO:2093 is the determined cDNA sequence of clone 61438505
SEQ ID NO:2094 is the determined cDNA sequence of clone 61438506
SEQ ID NO:2095 is the determined cDNA sequence of clone 61438507
30 SEQ ID NO:2096 is the determined cDNA sequence of clone 61438508
SEQ ID NO:2097 is the determined cDNA sequence of clone 61438509

SEQ ID NO:2098 is the determined cDNA sequence of clone 61438510
SEQ ID NO:2099 is the determined cDNA sequence of clone 61438512
SEQ ID NO:2100 is the determined cDNA sequence of clone 61438513
SEQ ID NO:2101 is the determined cDNA sequence of clone 61438514
5 SEQ ID NO:2102 is the determined cDNA sequence of clone 61438516
SEQ ID NO:2103 is the determined cDNA sequence of clone 61438518
SEQ ID NO:2104 is the determined cDNA sequence of clone 61438519
SEQ ID NO:2105 is the determined cDNA sequence of clone 61438520
SEQ ID NO:2106 is the determined cDNA sequence of clone 61438521
10 SEQ ID NO:2107 is the determined cDNA sequence of clone 61438522
SEQ ID NO:2108 is the determined cDNA sequence of clone 61438523
SEQ ID NO:2109 is the determined cDNA sequence of clone 61438524
SEQ ID NO:2110 is the determined cDNA sequence of clone 61438525
SEQ ID NO:2111 is the determined cDNA sequence of clone 61438527
15 SEQ ID NO:2112 is the determined cDNA sequence of clone 61438528
SEQ ID NO:2113 is the determined cDNA sequence of clone 61438530
SEQ ID NO:2114 is the determined cDNA sequence of clone 61438531
SEQ ID NO:2115 is the determined cDNA sequence of clone 61438533
SEQ ID NO:2116 is the determined cDNA sequence of clone 61438535
20 SEQ ID NO:2117 is the determined cDNA sequence of clone 61438536
SEQ ID NO:2118 is the determined cDNA sequence of clone 61438537
SEQ ID NO:2119 is the determined cDNA sequence of clone 61438538
SEQ ID NO:2120 is the determined cDNA sequence of clone 61438539
SEQ ID NO:2121 is the determined cDNA sequence of clone 61438540
25 SEQ ID NO:2122 is the determined cDNA sequence of clone 61438543
SEQ ID NO:2123 is the determined cDNA sequence of clone 61438544
SEQ ID NO:2124 is the determined cDNA sequence of clone 61438545
SEQ ID NO:2125 is the determined cDNA sequence of clone 61438547
SEQ ID NO:2126 is the determined cDNA sequence of clone 61438550
30 SEQ ID NO:2127 is the determined cDNA sequence of clone 61438551
SEQ ID NO:2128 is the determined cDNA sequence of clone 61438552

SEQ ID NO:2129 is the determined cDNA sequence of clone 61438553
SEQ ID NO:2130 is the determined cDNA sequence of clone 61438554
SEQ ID NO:2131 is the determined cDNA sequence of clone 61438555
SEQ ID NO:2132 is the determined cDNA sequence of clone 61438557
5 SEQ ID NO:2133 is the determined cDNA sequence of clone 61438558
SEQ ID NO:2134 is the determined cDNA sequence of clone 61438559
SEQ ID NO:2135 is the determined cDNA sequence of clone 61438560
SEQ ID NO:2136 is the determined cDNA sequence of clone 61438562
SEQ ID NO:2137 is the determined cDNA sequence of clone 61438563
10 SEQ ID NO:2138 is the determined cDNA sequence of clone 61438564
SEQ ID NO:2139 is the determined cDNA sequence of clone 61438565
SEQ ID NO:2140 is the determined cDNA sequence of clone 61438566
SEQ ID NO:2141 is the determined cDNA sequence of clone 61438567
SEQ ID NO:2142 is the determined cDNA sequence of clone 61438568
15 SEQ ID NO:2143 is the determined cDNA sequence of clone 61438569
SEQ ID NO:2144 is the determined cDNA sequence of clone 61438570
SEQ ID NO:2145 is the determined cDNA sequence of clone 61438571
SEQ ID NO:2146 is the determined cDNA sequence of clone 61438572
SEQ ID NO:2147 is the determined cDNA sequence of clone 61496495
20 SEQ ID NO:2148 is the determined cDNA sequence of clone 61496496
SEQ ID NO:2149 is the determined cDNA sequence of clone 61496497
SEQ ID NO:2150 is the determined cDNA sequence of clone 61496498
SEQ ID NO:2151 is the determined cDNA sequence of clone 61496500
SEQ ID NO:2152 is the determined cDNA sequence of clone 61496501
25 SEQ ID NO:2153 is the determined cDNA sequence of clone 61496502
SEQ ID NO:2154 is the determined cDNA sequence of clone 61496505
SEQ ID NO:2155 is the determined cDNA sequence of clone 61496508
SEQ ID NO:2156 is the determined cDNA sequence of clone 61496510
SEQ ID NO:2157 is the determined cDNA sequence of clone 61496511
30 SEQ ID NO:2158 is the determined cDNA sequence of clone 61496512
SEQ ID NO:2159 is the determined cDNA sequence of clone 61496513

SEQ ID NO:2160 is the determined cDNA sequence of clone 61496515
SEQ ID NO:2161 is the determined cDNA sequence of clone 61496516
SEQ ID NO:2162 is the determined cDNA sequence of clone 61496517
SEQ ID NO:2163 is the determined cDNA sequence of clone 61496518
5 SEQ ID NO:2164 is the determined cDNA sequence of clone 61496519
SEQ ID NO:2165 is the determined cDNA sequence of clone 61496520
SEQ ID NO:2166 is the determined cDNA sequence of clone 61496521
SEQ ID NO:2167 is the determined cDNA sequence of clone 61496522
SEQ ID NO:2168 is the determined cDNA sequence of clone 61496523
10 SEQ ID NO:2169 is the determined cDNA sequence of clone 61496524
SEQ ID NO:2170 is the determined cDNA sequence of clone 61496526
SEQ ID NO:2171 is the determined cDNA sequence of clone 61496528
SEQ ID NO:2172 is the determined cDNA sequence of clone 61496529
SEQ ID NO:2173 is the determined cDNA sequence of clone 61496530
15 SEQ ID NO:2174 is the determined cDNA sequence of clone 61496532
SEQ ID NO:2175 is the determined cDNA sequence of clone 61496534
SEQ ID NO:2176 is the determined cDNA sequence of clone 61496536
SEQ ID NO:2177 is the determined cDNA sequence of clone 61496537
SEQ ID NO:2178 is the determined cDNA sequence of clone 61496539
20 SEQ ID NO:2179 is the determined cDNA sequence of clone 61496543
SEQ ID NO:2180 is the determined cDNA sequence of clone 61496544
SEQ ID NO:2181 is the determined cDNA sequence of clone 61496545
SEQ ID NO:2182 is the determined cDNA sequence of clone 61496546
SEQ ID NO:2183 is the determined cDNA sequence of clone 61496547
25 SEQ ID NO:2184 is the determined cDNA sequence of clone 61496549
SEQ ID NO:2185 is the determined cDNA sequence of clone 61496551
SEQ ID NO:2186 is the determined cDNA sequence of clone 61496552
SEQ ID NO:2187 is the determined cDNA sequence of clone 61496553
SEQ ID NO:2188 is the determined cDNA sequence of clone 61496554
30 SEQ ID NO:2189 is the determined cDNA sequence of clone 61496555
SEQ ID NO:2190 is the determined cDNA sequence of clone 61496556

SEQ ID NO:2191 is the determined cDNA sequence of clone 61496557
SEQ ID NO:2192 is the determined cDNA sequence of clone 61496558
SEQ ID NO:2193 is the determined cDNA sequence of clone 61496559
SEQ ID NO:2194 is the determined cDNA sequence of clone 61496560
5 SEQ ID NO:2195 is the determined cDNA sequence of clone 61496561
SEQ ID NO:2196 is the determined cDNA sequence of clone 61496562
SEQ ID NO:2197 is the determined cDNA sequence of clone 61496564
SEQ ID NO:2198 is the determined cDNA sequence of clone 61496565
SEQ ID NO:2199 is the determined cDNA sequence of clone 61496566
10 SEQ ID NO:2200 is the determined cDNA sequence of clone 61496567
SEQ ID NO:2201 is the determined cDNA sequence of clone 61496568
SEQ ID NO:2202 is the determined cDNA sequence of clone 61496569
SEQ ID NO:2203 is the determined cDNA sequence of clone 61496570
SEQ ID NO:2204 is the determined cDNA sequence of clone 61496571
15 SEQ ID NO:2205 is the determined cDNA sequence of clone 61496572
SEQ ID NO:2206 is the determined cDNA sequence of clone 61496573
SEQ ID NO:2207 is the determined cDNA sequence of clone 61496574
SEQ ID NO:2208 is the determined cDNA sequence of clone 61496575
SEQ ID NO:2209 is the determined cDNA sequence of clone 61496576
20 SEQ ID NO:2210 is the determined cDNA sequence of clone 61496577
SEQ ID NO:2211 is the determined cDNA sequence of clone 61496578
SEQ ID NO:2212 is the determined cDNA sequence of clone 61496581
SEQ ID NO:2213 is the determined cDNA sequence of clone 61496582
SEQ ID NO:2214 is the determined cDNA sequence of clone 61496583
25 SEQ ID NO:2215 is the determined cDNA sequence of clone 61496584
SEQ ID NO:2216 is the determined cDNA sequence of clone 61496585
SEQ ID NO:2217 is the determined cDNA sequence of clone 61496586
SEQ ID NO:2218 is the determined cDNA sequence of clone 61496587
SEQ ID NO:2219 is the determined cDNA sequence of clone 61496700
30 SEQ ID NO:2220 is the determined cDNA sequence of clone 61496701
SEQ ID NO:2221 is the determined cDNA sequence of clone 61496702

SEQ ID NO:2222 is the determined cDNA sequence of clone 61496704
SEQ ID NO:2223 is the determined cDNA sequence of clone 61496705
SEQ ID NO:2224 is the determined cDNA sequence of clone 61496709
SEQ ID NO:2225 is the determined cDNA sequence of clone 61496710
5 SEQ ID NO:2226 is the determined cDNA sequence of clone 61496713
SEQ ID NO:2227 is the determined cDNA sequence of clone 61496715
SEQ ID NO:2228 is the determined cDNA sequence of clone 61496716
SEQ ID NO:2229 is the determined cDNA sequence of clone 61496717
SEQ ID NO:2230 is the determined cDNA sequence of clone 61496718
10 SEQ ID NO:2231 is the determined cDNA sequence of clone 61496719
SEQ ID NO:2232 is the determined cDNA sequence of clone 61496720
SEQ ID NO:2233 is the determined cDNA sequence of clone 61496721
SEQ ID NO:2234 is the determined cDNA sequence of clone 61496722
SEQ ID NO:2235 is the determined cDNA sequence of clone 61496723
15 SEQ ID NO:2236 is the determined cDNA sequence of clone 61496725
SEQ ID NO:2237 is the determined cDNA sequence of clone 61496726
SEQ ID NO:2238 is the determined cDNA sequence of clone 61496727
SEQ ID NO:2239 is the determined cDNA sequence of clone 61496729
SEQ ID NO:2240 is the determined cDNA sequence of clone 61496731
20 SEQ ID NO:2241 is the determined cDNA sequence of clone 61496733
SEQ ID NO:2242 is the determined cDNA sequence of clone 61496735
SEQ ID NO:2243 is the determined cDNA sequence of clone 61496737
SEQ ID NO:2244 is the determined cDNA sequence of clone 61496738
SEQ ID NO:2245 is the determined cDNA sequence of clone 61496739
25 SEQ ID NO:2246 is the determined cDNA sequence of clone 61496740
SEQ ID NO:2247 is the determined cDNA sequence of clone 61496741
SEQ ID NO:2248 is the determined cDNA sequence of clone 61496743
SEQ ID NO:2249 is the determined cDNA sequence of clone 61496745
SEQ ID NO:2250 is the determined cDNA sequence of clone 61496746
30 SEQ ID NO:2251 is the determined cDNA sequence of clone 61496747
SEQ ID NO:2252 is the determined cDNA sequence of clone 61496748

SEQ ID NO:2253 is the determined cDNA sequence of clone 61496749
SEQ ID NO:2254 is the determined cDNA sequence of clone 61496750
SEQ ID NO:2255 is the determined cDNA sequence of clone 61496751
SEQ ID NO:2256 is the determined cDNA sequence of clone 61496753
5 SEQ ID NO:2257 is the determined cDNA sequence of clone 61496754
SEQ ID NO:2258 is the determined cDNA sequence of clone 61496756
SEQ ID NO:2259 is the determined cDNA sequence of clone 61496757
SEQ ID NO:2260 is the determined cDNA sequence of clone 61496758
SEQ ID NO:2261 is the determined cDNA sequence of clone 61496759
10 SEQ ID NO:2262 is the determined cDNA sequence of clone 61496761
SEQ ID NO:2263 is the determined cDNA sequence of clone 61496762
SEQ ID NO:2264 is the determined cDNA sequence of clone 61496763
SEQ ID NO:2265 is the determined cDNA sequence of clone 61496764
SEQ ID NO:2266 is the determined cDNA sequence of clone 61496765
15 SEQ ID NO:2267 is the determined cDNA sequence of clone 61496766
SEQ ID NO:2268 is the determined cDNA sequence of clone 61496768
SEQ ID NO:2269 is the determined cDNA sequence of clone 61496769
SEQ ID NO:2270 is the determined cDNA sequence of clone 61496770
SEQ ID NO:2271 is the determined cDNA sequence of clone 61496771
20 SEQ ID NO:2272 is the determined cDNA sequence of clone 61496772
SEQ ID NO:2273 is the determined cDNA sequence of clone 61496774
SEQ ID NO:2274 is the determined cDNA sequence of clone 61496776
SEQ ID NO:2275 is the determined cDNA sequence of clone 61496777
SEQ ID NO:2276 is the determined cDNA sequence of clone 61496778
25 SEQ ID NO:2277 is the determined cDNA sequence of clone 61496780
SEQ ID NO:2278 is the determined cDNA sequence of clone 61496781
SEQ ID NO:2279 is the determined cDNA sequence of clone 61496782
SEQ ID NO:2280 is the determined cDNA sequence of clone 61496783
SEQ ID NO:2281 is the determined cDNA sequence of clone 61496784
30 SEQ ID NO:2282 is the determined cDNA sequence of clone 61496785
SEQ ID NO:2283 is the determined cDNA sequence of clone 61496786

SEQ ID NO:2284 is the determined cDNA sequence of clone 61496787
SEQ ID NO:2285 is the determined cDNA sequence of clone 61496788
SEQ ID NO:2286 is the determined cDNA sequence of clone 61496789
SEQ ID NO:2287 is the determined cDNA sequence of clone 61496790
5 SEQ ID NO:2288 is the determined cDNA sequence of clone 61497422
SEQ ID NO:2289 is the determined cDNA sequence of clone 61497424
SEQ ID NO:2290 is the determined cDNA sequence of clone 61497425
SEQ ID NO:2291 is the determined cDNA sequence of clone 61497426
SEQ ID NO:2292 is the determined cDNA sequence of clone 61497429
10 SEQ ID NO:2293 is the determined cDNA sequence of clone 61497430
SEQ ID NO:2294 is the determined cDNA sequence of clone 61497432
SEQ ID NO:2295 is the determined cDNA sequence of clone 61497433
SEQ ID NO:2296 is the determined cDNA sequence of clone 61497435
SEQ ID NO:2297 is the determined cDNA sequence of clone 61497436
15 SEQ ID NO:2298 is the determined cDNA sequence of clone 61497437
SEQ ID NO:2299 is the determined cDNA sequence of clone 61497438
SEQ ID NO:2300 is the determined cDNA sequence of clone 61497439
SEQ ID NO:2301 is the determined cDNA sequence of clone 61497440
SEQ ID NO:2302 is the determined cDNA sequence of clone 61497441
20 SEQ ID NO:2303 is the determined cDNA sequence of clone 61497443
SEQ ID NO:2304 is the determined cDNA sequence of clone 61497444
SEQ ID NO:2305 is the determined cDNA sequence of clone 61497446
SEQ ID NO:2306 is the determined cDNA sequence of clone 61497447
SEQ ID NO:2307 is the determined cDNA sequence of clone 61497448
25 SEQ ID NO:2308 is the determined cDNA sequence of clone 61497450
SEQ ID NO:2309 is the determined cDNA sequence of clone 61497451
SEQ ID NO:2310 is the determined cDNA sequence of clone 61497452
SEQ ID NO:2311 is the determined cDNA sequence of clone 61497454
SEQ ID NO:2312 is the determined cDNA sequence of clone 61497455
30 SEQ ID NO:2313 is the determined cDNA sequence of clone 61497456
SEQ ID NO:2314 is the determined cDNA sequence of clone 61497457

SEQ ID NO:2315 is the determined cDNA sequence of clone 61497458
SEQ ID NO:2316 is the determined cDNA sequence of clone 61497459
SEQ ID NO:2317 is the determined cDNA sequence of clone 61497460
SEQ ID NO:2318 is the determined cDNA sequence of clone 61497462
5 SEQ ID NO:2319 is the determined cDNA sequence of clone 61497463
SEQ ID NO:2320 is the determined cDNA sequence of clone 61497464
SEQ ID NO:2321 is the determined cDNA sequence of clone 61497466
SEQ ID NO:2322 is the determined cDNA sequence of clone 61497468
SEQ ID NO:2323 is the determined cDNA sequence of clone 61497469
10 SEQ ID NO:2324 is the determined cDNA sequence of clone 61497470
SEQ ID NO:2325 is the determined cDNA sequence of clone 61497471
SEQ ID NO:2326 is the determined cDNA sequence of clone 61497473
SEQ ID NO:2327 is the determined cDNA sequence of clone 61497474
SEQ ID NO:2328 is the determined cDNA sequence of clone 61497477
15 SEQ ID NO:2329 is the determined cDNA sequence of clone 61497478
SEQ ID NO:2330 is the determined cDNA sequence of clone 61497479
SEQ ID NO:2331 is the determined cDNA sequence of clone 61497480
SEQ ID NO:2332 is the determined cDNA sequence of clone 61497481
SEQ ID NO:2333 is the determined cDNA sequence of clone 61497482
20 SEQ ID NO:2334 is the determined cDNA sequence of clone 61497483
SEQ ID NO:2335 is the determined cDNA sequence of clone 61497484
SEQ ID NO:2336 is the determined cDNA sequence of clone 61497486
SEQ ID NO:2337 is the determined cDNA sequence of clone 61497487
SEQ ID NO:2338 is the determined cDNA sequence of clone 61497488
25 SEQ ID NO:2339 is the determined cDNA sequence of clone 61497489
SEQ ID NO:2340 is the determined cDNA sequence of clone 61497490
SEQ ID NO:2341 is the determined cDNA sequence of clone 61497491
SEQ ID NO:2342 is the determined cDNA sequence of clone 61497493
SEQ ID NO:2343 is the determined cDNA sequence of clone 61497494
30 SEQ ID NO:2344 is the determined cDNA sequence of clone 61497495
SEQ ID NO:2345 is the determined cDNA sequence of clone 61497496

SEQ ID NO:2346 is the determined cDNA sequence of clone 61497497
SEQ ID NO:2347 is the determined cDNA sequence of clone 61497498
SEQ ID NO:2348 is the determined cDNA sequence of clone 61497499
SEQ ID NO:2349 is the determined cDNA sequence of clone 61497500
5 SEQ ID NO:2350 is the determined cDNA sequence of clone 61497501
SEQ ID NO:2351 is the determined cDNA sequence of clone 61497502
SEQ ID NO:2352 is the determined cDNA sequence of clone 61497503
SEQ ID NO:2353 is the determined cDNA sequence of clone 61497504
SEQ ID NO:2354 is the determined cDNA sequence of clone 61497505
10 SEQ ID NO:2355 is the determined cDNA sequence of clone 61497507
SEQ ID NO:2356 is the determined cDNA sequence of clone 61497509
SEQ ID NO:2357 is the determined cDNA sequence of clone 61497511
SEQ ID NO:2358 is the determined cDNA sequence of clone 61497512
SEQ ID NO:2359 is the determined cDNA sequence of clone 61497513
15 SEQ ID NO:2360 is the determined cDNA sequence of clone 61497514
SEQ ID NO:2361 is the determined cDNA sequence of clone 61497515
SEQ ID NO:2362 is the determined cDNA sequence of clone 61497516
SEQ ID NO:2363 is the determined cDNA sequence of clone 61497517
SEQ ID NO:2364 is the determined cDNA sequence of clone 61497518
20 SEQ ID NO:2365 is the determined cDNA sequence of clone 61497519
SEQ ID NO:2366 is the determined cDNA sequence of clone 61497520
SEQ ID NO:2367 is the determined cDNA sequence of clone 61497521
SEQ ID NO:2368 is the determined cDNA sequence of clone 61497522
SEQ ID NO:2369 is the determined cDNA sequence of clone 61497523
25 SEQ ID NO:2370 is the determined cDNA sequence of clone 61497524
SEQ ID NO:2371 is the determined cDNA sequence of clone 61497526
SEQ ID NO:2372 is the determined cDNA sequence of clone 61497527
SEQ ID NO:2373 is the determined cDNA sequence of clone 61497528
SEQ ID NO:2374 is the determined cDNA sequence of clone 61497529
30 SEQ ID NO:2375 is the determined cDNA sequence of clone 61497530
SEQ ID NO:2376 is the determined cDNA sequence of clone 61497531

SEQ ID NO:2377 is the determined cDNA sequence of clone 61497532
SEQ ID NO:2378 is the determined cDNA sequence of clone 61497533
SEQ ID NO:2379 is the determined cDNA sequence of clone 61497534
SEQ ID NO:2380 is the determined cDNA sequence of clone 61497535
5 SEQ ID NO:2381 is the determined cDNA sequence of clone 61497536
SEQ ID NO:2382 is the determined cDNA sequence of clone 61497537
SEQ ID NO:2383 is the determined cDNA sequence of clone 61497538
SEQ ID NO:2384 is the determined cDNA sequence of clone 61497539
SEQ ID NO:2385 is the determined cDNA sequence of clone 61497540
10 SEQ ID NO:2386 is the determined cDNA sequence of clone 61497541
SEQ ID NO:2387 is the determined cDNA sequence of clone 61497542
SEQ ID NO:2388 is the determined cDNA sequence of clone 61497543
SEQ ID NO:2389 is the determined cDNA sequence of clone 61497544
SEQ ID NO:2390 is the determined cDNA sequence of clone 61497545
15 SEQ ID NO:2391 is the determined cDNA sequence of clone 61497546
SEQ ID NO:2392 is the determined cDNA sequence of clone 61497547
SEQ ID NO:2393 is the determined cDNA sequence of clone 61497549
SEQ ID NO:2394 is the determined cDNA sequence of clone 61497551
SEQ ID NO:2395 is the determined cDNA sequence of clone 61497552
20 SEQ ID NO:2396 is the determined cDNA sequence of clone 61497553
SEQ ID NO:2397 is the determined cDNA sequence of clone 61497554
SEQ ID NO:2398 is the determined cDNA sequence of clone 61497556
SEQ ID NO:2399 is the determined cDNA sequence of clone 61497557
SEQ ID NO:2400 is the determined cDNA sequence of clone 61497560
25 SEQ ID NO:2401 is the determined cDNA sequence of clone 61497561
SEQ ID NO:2402 is the determined cDNA sequence of clone 61497562
SEQ ID NO:2403 is the determined cDNA sequence of clone 61497563
SEQ ID NO:2404 is the determined cDNA sequence of clone 61497564
SEQ ID NO:2405 is the determined cDNA sequence of clone 61497565
30 SEQ ID NO:2406 is the determined cDNA sequence of clone 61497566
SEQ ID NO:2407 is the determined cDNA sequence of clone 61497567

SEQ ID NO:2408 is the determined cDNA sequence of clone 61497568
SEQ ID NO:2409 is the determined cDNA sequence of clone 61497569
SEQ ID NO:2410 is the determined cDNA sequence of clone 61497570
SEQ ID NO:2411 is the determined cDNA sequence of clone 61497571
5 SEQ ID NO:2412 is the determined cDNA sequence of clone 61497572
SEQ ID NO:2413 is the determined cDNA sequence of clone 61497574
SEQ ID NO:2414 is the determined cDNA sequence of clone 61497575
SEQ ID NO:2415 is the determined cDNA sequence of clone 61497576
SEQ ID NO:2416 is the determined cDNA sequence of clone 61497577
10 SEQ ID NO:2417 is the determined cDNA sequence of clone 61497578
SEQ ID NO:2418 is the determined cDNA sequence of clone 61497579
SEQ ID NO:2419 is the determined cDNA sequence of clone 61497580
SEQ ID NO:2420 is the determined cDNA sequence of clone 61497581
SEQ ID NO:2421 is the determined cDNA sequence of clone 61497582
15 SEQ ID NO:2422 is the determined cDNA sequence of clone 61497583
SEQ ID NO:2423 is the determined cDNA sequence of clone 61497584
SEQ ID NO:2424 is the determined cDNA sequence of clone 61497585
SEQ ID NO:2425 is the determined cDNA sequence of clone 61497587
SEQ ID NO:2426 is the determined cDNA sequence of clone 61497588
20 SEQ ID NO:2427 is the determined cDNA sequence of clone 61497589
SEQ ID NO:2428 is the determined cDNA sequence of clone 61497590
SEQ ID NO:2429 is the determined cDNA sequence of clone 61497591
SEQ ID NO:2430 is the determined cDNA sequence of clone 61497592
SEQ ID NO:2431 is the determined cDNA sequence of clone 61497593
25 SEQ ID NO:2432 is the determined cDNA sequence of clone 61497594
SEQ ID NO:2433 is the determined cDNA sequence of clone 61497595
SEQ ID NO:2434 is the determined cDNA sequence of clone 61497596
SEQ ID NO:2435 is the determined cDNA sequence of clone 61497597
SEQ ID NO:2436 is the determined cDNA sequence of clone 61497598
30 SEQ ID NO:2437 is the determined cDNA sequence of clone 61497599
SEQ ID NO:2438 is the determined cDNA sequence of clone 61497600

SEQ ID NO:2439 is the determined cDNA sequence of clone 61497601
SEQ ID NO:2440 is the determined cDNA sequence of clone 61497602
SEQ ID NO:2441 is the determined cDNA sequence of clone 61497603
SEQ ID NO:2442 is the determined cDNA sequence of clone 61497604
5 SEQ ID NO:2443 is the determined cDNA sequence of clone 61497605
SEQ ID NO:2444 is the determined cDNA sequence of clone 61497606
SEQ ID NO:2445 is the determined cDNA sequence of clone 61497607
SEQ ID NO:2446 is the determined cDNA sequence of clone 61497608
SEQ ID NO:2447 is the determined cDNA sequence of clone 61497609
10 SEQ ID NO:2448 is the determined cDNA sequence of clone 61497610
SEQ ID NO:2449 is the determined cDNA sequence of clone 61497615
SEQ ID NO:2450 is the determined cDNA sequence of clone 61497616
SEQ ID NO:2451 is the determined cDNA sequence of clone 61497618
SEQ ID NO:2452 is the determined cDNA sequence of clone 61497619
15 SEQ ID NO:2453 is the determined cDNA sequence of clone 61497623
SEQ ID NO:2454 is the determined cDNA sequence of clone 61497624
SEQ ID NO:2455 is the determined cDNA sequence of clone 61497625
SEQ ID NO:2456 is the determined cDNA sequence of clone 61497626
SEQ ID NO:2457 is the determined cDNA sequence of clone 61497627
20 SEQ ID NO:2458 is the determined cDNA sequence of clone 61497628
SEQ ID NO:2459 is the determined cDNA sequence of clone 61497630
SEQ ID NO:2460 is the determined cDNA sequence of clone 61497631
SEQ ID NO:2461 is the determined cDNA sequence of clone 61497632
SEQ ID NO:2462 is the determined cDNA sequence of clone 61497633
25 SEQ ID NO:2463 is the determined cDNA sequence of clone 61497635
SEQ ID NO:2464 is the determined cDNA sequence of clone 61497636
SEQ ID NO:2465 is the determined cDNA sequence of clone 61497637
SEQ ID NO:2466 is the determined cDNA sequence of clone 61497638
SEQ ID NO:2467 is the determined cDNA sequence of clone 61497639
30 SEQ ID NO:2468 is the determined cDNA sequence of clone 61497640
SEQ ID NO:2469 is the determined cDNA sequence of clone 6149764I

SEQ ID NO:2470 is the determined cDNA sequence of clone 61497643
SEQ ID NO:2471 is the determined cDNA sequence of clone 61497645
SEQ ID NO:2472 is the determined cDNA sequence of clone 61497646
SEQ ID NO:2473 is the determined cDNA sequence of clone 61497648
5 SEQ ID NO:2474 is the determined cDNA sequence of clone 61497649
SEQ ID NO:2475 is the determined cDNA sequence of clone 61497650
SEQ ID NO:2476 is the determined cDNA sequence of clone 61497652
SEQ ID NO:2477 is the determined cDNA sequence of clone 61497653
SEQ ID NO:2478 is the determined cDNA sequence of clone 61497655
10 SEQ ID NO:2479 is the determined cDNA sequence of clone 61497656
SEQ ID NO:2480 is the determined cDNA sequence of clone 61497657
SEQ ID NO:2481 is the determined cDNA sequence of clone 61497659
SEQ ID NO:2482 is the determined cDNA sequence of clone 61497660
SEQ ID NO:2483 is the determined cDNA sequence of clone 61497661
15 SEQ ID NO:2484 is the determined cDNA sequence of clone 61497662
SEQ ID NO:2485 is the determined cDNA sequence of clone 61497663
SEQ ID NO:2486 is the determined cDNA sequence of clone 61497664
SEQ ID NO:2487 is the determined cDNA sequence of clone 61497665
SEQ ID NO:2488 is the determined cDNA sequence of clone 61497666
20 SEQ ID NO:2489 is the determined cDNA sequence of clone 61497669
SEQ ID NO:2490 is the determined cDNA sequence of clone 61497670
SEQ ID NO:2491 is the determined cDNA sequence of clone 61497671
SEQ ID NO:2492 is the determined cDNA sequence of clone 61497673
SEQ ID NO:2493 is the determined cDNA sequence of clone 61497675
25 SEQ ID NO:2494 is the determined cDNA sequence of clone 61497676
SEQ ID NO:2495 is the determined cDNA sequence of clone 61497677
SEQ ID NO:2496 is the determined cDNA sequence of clone 61497678
SEQ ID NO:2497 is the determined cDNA sequence of clone 61497681
SEQ ID NO:2498 is the determined cDNA sequence of clone 61497682
30 SEQ ID NO:2499 is the determined cDNA sequence of clone 61497683
SEQ ID NO:2500 is the determined cDNA sequence of clone 61497684

SEQ ID NO:2501 is the determined cDNA sequence of clone 61497686
SEQ ID NO:2502 is the determined cDNA sequence of clone 61497687
SEQ ID NO:2503 is the determined cDNA sequence of clone 61497688
SEQ ID NO:2504 is the determined cDNA sequence of clone 61497691
5 SEQ ID NO:2505 is the determined cDNA sequence of clone 61497694
SEQ ID NO:2506 is the determined cDNA sequence of clone 61497695
SEQ ID NO:2507 is the determined cDNA sequence of clone 61524967
SEQ ID NO:2508 is the determined cDNA sequence of clone 61524969
SEQ ID NO:2509 is the determined cDNA sequence of clone 61524970
10 SEQ ID NO:2510 is the determined cDNA sequence of clone 61524971
SEQ ID NO:2511 is the determined cDNA sequence of clone 61524975
SEQ ID NO:2512 is the determined cDNA sequence of clone 61524976
SEQ ID NO:2513 is the determined cDNA sequence of clone 61524977
SEQ ID NO:2514 is the determined cDNA sequence of clone 61524979
15 SEQ ID NO:2515 is the determined cDNA sequence of clone 61524982
SEQ ID NO:2516 is the determined cDNA sequence of clone 61524983
SEQ ID NO:2517 is the determined cDNA sequence of clone 61524985
SEQ ID NO:2518 is the determined cDNA sequence of clone 61524986
SEQ ID NO:2519 is the determined cDNA sequence of clone 61524987
20 SEQ ID NO:2520 is the determined cDNA sequence of clone 61524988
SEQ ID NO:2521 is the determined cDNA sequence of clone 61524989
SEQ ID NO:2522 is the determined cDNA sequence of clone 61524990
SEQ ID NO:2523 is the determined cDNA sequence of clone 61524991
SEQ ID NO:2524 is the determined cDNA sequence of clone 61524993
25 SEQ ID NO:2525 is the determined cDNA sequence of clone 61524994
SEQ ID NO:2526 is the determined cDNA sequence of clone 61524995
SEQ ID NO:2527 is the determined cDNA sequence of clone 61524996
SEQ ID NO:2528 is the determined cDNA sequence of clone 61524997
SEQ ID NO:2529 is the determined cDNA sequence of clone 61524999
30 SEQ ID NO:2530 is the determined cDNA sequence of clone 61525000
SEQ ID NO:2531 is the determined cDNA sequence of clone 61525001

SEQ ID NO:2532 is the determined cDNA sequence of clone 61525003
SEQ ID NO:2533 is the determined cDNA sequence of clone 61525004
SEQ ID NO:2534 is the determined cDNA sequence of clone 61525005
SEQ ID NO:2535 is the determined cDNA sequence of clone 61525006
5 SEQ ID NO:2536 is the determined cDNA sequencne of clone 61525007
SEQ ID NO:2537 is the determined cDNA sequence of clone 61525008
SEQ ID NO:2538 is the determined cDNA sequence of clone 61525009
SEQ ID NO:2539 is the determined cDNA sequence of clone 61525011
SEQ ID NO:2540 is the determined cDNA sequence of clone 61525013
10 SEQ ID NO:2541 is the determined cDNA sequence of clone 61525014
SEQ ID NO:2542 is the determined cDNA sequence of clone 61525015
SEQ ID NO:2543 is the determined cDNA sequence of clone 61525017
SEQ ID NO:2544 is the determined cDNA sequence of clone 61525020
SEQ ID NO:2545 is the determined cDNA sequence of clone 61525021
15 SEQ ID NO:2546 is the determined cDNA sequence of clone 61525022
SEQ ID NO:2547 is the determined cDNA sequence of clone 61525023
SEQ ID NO:2548 is the determined cDNA sequence of clone 61525026
SEQ ID NO:2549 is the determined cDNA sequence of clone 61525027
SEQ ID NO:2550 is the determined cDNA sequence of clone 61525029
20 SEQ ID NO:2551 is the determined cDNA sequence of clone 61525031
SEQ ID NO:2552 is the determined cDNA sequence of clone 61525034
SEQ ID NO:2553 is the determined cDNA sequence of clone 61525035
SEQ ID NO:2554 is the determined cDNA sequence of clone 61525038
SEQ ID NO:2555 is the dtermined cDNA sequence of clone 61525039
25 SEQ ID NO:2556 is the determined cDNA sequence of clone 61525040
SEQ ID NO:2557 is the determined cDNA sequence of clone 61525041
SEQ ID NO:2558 is the determined cDNA sequence of clone 61525042
SEQ ID NO:2559 is the determined cDNA sequence of clone 61525043
SEQ ID NO:2560 is the determined cDNA sequence of clone 61525044
30 SEQ ID NO:2561 is the determined cDNA sequence of clone 61525045
SEQ ID NO:2562 is the determined cDNA sequence of clone 61525047

SEQ ID NO:2563 is the determined cDNA sequence of clone 61525048
SEQ ID NO:2564 is the determined cDNA sequence of clone 61525049
SEQ ID NO:2565 is the determined cDNA sequence of clone 61525050
SEQ ID NO:2566 is the determined cDNA sequence of clone 61525052
5 SEQ ID NO:2567 is the determined cDNA sequence of clone 61525054
SEQ ID NO:2568 is the determined cDNA sequence of clone 61525055
SEQ ID NO:2569 is the determined cDNA sequence of clone 61525057
SEQ ID NO:2570 is the determined cDNA sequence of clone 61546433
SEQ ID NO:2571 is the determined cDNA sequence of clone 61546435
10 SEQ ID NO:2572 is the determined cDNA sequence of clone 61546436
SEQ ID NO:2573 is the determined cDNA sequence of clone 61546437
SEQ ID NO:2574 is the determined cDNA sequence of clone 61546439
SEQ ID NO:2575 is the determined cDNA sequence of clone 61546440
SEQ ID NO:2576 is the determined cDNA sequence of clone 61546442
15 SEQ ID NO:2577 is the determined cDNA sequence of clone 61546443
SEQ ID NO:2578 is the determined cDNA sequence of clone 61546444
SEQ ID NO:2579 is the determined cDNA sequence of clone 61546446
SEQ ID NO:2580 is the determined cDNA sequence of clone 61546447
SEQ ID NO:2581 is the determined cDNA sequence of clone 61546450
20 SEQ ID NO:2582 is the determined cDNA sequence of clone 61546451
SEQ ID NO:2583 is the determined cDNA sequence of clone 61546454
SEQ ID NO:2584 is the determined cDNA sequence of clone 61546455
SEQ ID NO:2585 is the determined cDNA sequence of clone 61546457
SEQ ID NO:2586 is the determined cDNA sequence of clone 61546458
25 SEQ ID NO:2587 is the determined cDNA sequence of clone 61546460
SEQ ID NO:2588 is the determined cDNA sequence of clone 61546461
SEQ ID NO:2589 is the determined cDNA sequence of clone 61546462
SEQ ID NO:2590 is the determined cDNA sequence of clone 61546463
SEQ ID NO:2591 is the determined cDNA sequence of clone 61546465
30 SEQ ID NO:2592 is the determined cDNA sequence of clone 61546466
SEQ ID NO:2593 is the determined cDNA sequence of clone 61546469

SEQ ID NO:2594 is the determined cDNA sequence of clone 61546471
SEQ ID NO:2595 is the determined cDNA sequence of clone 61546472
SEQ ID NO:2596 is the determined cDNA sequence of clone 61546473
SEQ ID NO:2597 is the determined cDNA sequence of clone 61546474
5 SEQ ID NO:2598 is the determined cDNA sequence of clone 61546475
SEQ ID NO:2599 is the determined cDNA sequence of clone 61546476
SEQ ID NO:2600 is the determined cDNA sequence of clone 61546477
SEQ ID NO:2601 is the determined cDNA sequence of clone 61546478
SEQ ID NO:2602 is the determined cDNA sequence of clone 61546480
10 SEQ ID NO:2603 is the determined cDNA sequence of clone 61546481
SEQ ID NO:2604 is the determined cDNA sequence of clone 61546482
SEQ ID NO:2605 is the determined cDNA sequence of clone 61546484
SEQ ID NO:2606 is the determined cDNA sequence of clone 61546487
SEQ ID NO:2607 is the determined cDNA sequence of clone 61546488
15 SEQ ID NO:2608 is the determined cDNA sequence of clone 61546490
SEQ ID NO:2609 is the determined cDNA sequence of clone 61546491
SEQ ID NO:2610 is the determined cDNA sequence of clone 61546492
SEQ ID NO:2611 is the determined cDNA sequence of clone 61546493
SEQ ID NO:2612 is the determined cDNA sequence of clone 61546496
20 SEQ ID NO:2613 is the determined cDNA sequence of clone 61546497
SEQ ID NO:2614 is the determined cDNA sequence of clone 61546498
SEQ ID NO:2615 is the determined cDNA sequence of clone 61546499
SEQ ID NO:2616 is the determined cDNA sequence of clone 61546500
SEQ ID NO:2617 is the determined cDNA sequence of clone 61546502
25 SEQ ID NO:2618 is the determined cDNA sequence of clone 61546503
SEQ ID NO:2619 is the determined cDNA sequence of clone 61546505
SEQ ID NO:2620 is the determined cDNA sequence of clone 61546507
SEQ ID NO:2621 is the determined cDNA sequence of clone 61546508
SEQ ID NO:2622 is the determined cDNA sequence of clone 61546509
30 SEQ ID NO:2623 is the determined cDNA sequence of clone 61546510
SEQ ID NO:2624 is the determined cDNA sequence of clone 61546512

SEQ ID NO:2625 is the determined cDNA sequence of clone 61546513
SEQ ID NO:2626 is the determined cDNA sequence of clone 61546516
SEQ ID NO:2627 is the determined cDNA sequence of clone 61546517
SEQ ID NO:2628 is the determined cDNA sequence of clone 61546518
5 SEQ ID NO:2629 is the determined cDNA sequence of clone 61546519
SEQ ID NO:2630 is the determined cDNA sequence of clone 61546520
SEQ ID NO:2631 is the determined cDNA sequence of clone 61546521
SEQ ID NO:2632 is the determined cDNA sequence of clone 61546522
SEQ ID NO:2633 is the determined cDNA sequence of clone 61546523
10 SEQ ID NO:2634 is the determined cDNA sequence of clone 61546524
SEQ ID NO:2635 is the determined cDNA sequence of clone 61814355
SEQ ID NO:2636 is the determined cDNA sequence of clone 61814356
SEQ ID NO:2637 is the determined cDNA sequence of clone 61814357
SEQ ID NO:2638 is the determined cDNA sequence of clone 61814360
15 SEQ ID NO:2639 is the determined cDNA sequence of clone 61814361
SEQ ID NO:2640 is the determined cDNA sequence of clone 61814362
SEQ ID NO:2641 is the determined cDNA sequence of clone 61814363
SEQ ID NO:2642 is the determined cDNA sequence of clone 61814364
SEQ ID NO:2643 is the determined cDNA sequence of clone 61814365
20 SEQ ID NO:2644 is the determined cDNA sequence of clone 61814366
SEQ ID NO:2645 is the determined cDNA sequence of clone 61814368
SEQ ID NO:2646 is the determined cDNA sequence of clone 61814369
SEQ ID NO:2647 is the determined cDNA sequence of clone 61814370
SEQ ID NO:2648 is the determined cDNA sequence of clone 61814371
25 SEQ ID NO:2649 is the determined cDNA sequence of clone 61814372
SEQ ID NO:2650 is the determined cDNA sequence of clone 61814373
SEQ ID NO:2651 is the determined cDNA sequence of clone 61814374
SEQ ID NO:2652 is the determined cDNA sequence of clone 61814376
SEQ ID NO:2653 is the determined cDNA sequence of clone 61814377
30 SEQ ID NO:2654 is the determined cDNA sequence of clone 61814378
SEQ ID NO:2655 is the determined cDNA sequence of clone 61814379

SEQ ID NO:2656 is the determined cDNA sequence of clone 61814381
SEQ ID NO:2657 is the determined cDNA sequence of clone 61814382
SEQ ID NO:2658 is the determined cDNA sequence of clone 61814383
SEQ ID NO:2659 is the determined cDNA sequence of clone 61814384
5 SEQ ID NO:2660 is the determined cDNA sequence of clone 61814385
SEQ ID NO:2661 is the determined cDNA sequence of clone 61814386
SEQ ID NO:2662 is the determined cDNA sequence of clone 61814387
SEQ ID NO:2663 is the determined cDNA sequence of clone 61814388
SEQ ID NO:2664 is the determined cDNA sequence of clone 61814389
10 SEQ ID NO:2665 is the determined cDNA sequence of clone 61814390
SEQ ID NO:2666 is the determined cDNA sequence of clone 61814391
SEQ ID NO:2667 is the determined cDNA sequence of clone 61814393
SEQ ID NO:2668 is the determined cDNA sequence of clone 61814394
SEQ ID NO:2669 is the determined cDNA sequence of clone 61814395
15 SEQ ID NO:2670 is the determined cDNA sequence of clone 61814396
SEQ ID NO:2671 is the determined cDNA sequence of clone 61814397
SEQ ID NO:2672 is the determined cDNA sequence of clone 61814398
SEQ ID NO:2673 is the determined cDNA sequence of clone 61814399
SEQ ID NO:2674 is the determined cDNA sequence of clone 61814400
20 SEQ ID NO:2675 is the determined cDNA sequence of clone 61814401
SEQ ID NO:2676 is the determined cDNA sequence of clone 61814402
SEQ ID NO:2677 is the determined cDNA sequence of clone 61814403
SEQ ID NO:2678 is the determined cDNA sequence of clone 61814405
SEQ ID NO:2679 is the determined cDNA sequence of clone 61814406
25 SEQ ID NO:2680 is the determined cDNA sequence of clone 61814407
SEQ ID NO:2681 is the determined cDNA sequence of clone 61814408
SEQ ID NO:2682 is the determined cDNA sequence of clone 61814409
SEQ ID NO:2683 is the determined cDNA sequence of clone 61814410
SEQ ID NO:2684 is the determined cDNA sequence of clone 61814411
30 SEQ ID NO:2685 is the determined cDNA sequence of clone 61814413
SEQ ID NO:2686 is the determined cDNA sequence of clone 61814414

SEQ ID NO:2687 is the determined cDNA sequence of clone 61814415
SEQ ID NO:2688 is the determined cDNA sequence of clone 61814416
SEQ ID NO:2689 is the determined cDNA sequence of clone 61814418
SEQ ID NO:2690 is the determined cDNA sequence of clone 61814419
5 SEQ ID NO:2691 is the determined cDNA sequence of clone 61814420
SEQ ID NO:2692 is the determined cDNA sequence of clone 61814421
SEQ ID NO:2693 is the determined cDNA sequence of clone 61814422
SEQ ID NO:2694 is the determined cDNA sequence of clone 61814423
SEQ ID NO:2695 is the determined cDNA sequence of clone 61814424
10 SEQ ID NO:2696 is the determined cDNA sequence of clone 61814426
SEQ ID NO:2697 is the determined cDNA sequence of clone 61814427
SEQ ID NO:2698 is the determined cDNA sequence of clone 61814428
SEQ ID NO:2699 is the determined cDNA sequence of clone 61814429
SEQ ID NO:2700 is the determined cDNA sequence of clone 61814431
15 SEQ ID NO:2701 is the determined cDNA sequence of clone 61814433
SEQ ID NO:2702 is the determined cDNA sequence of clone 61814434
SEQ ID NO:2703 is the determined cDNA sequence of clone 61814435
SEQ ID NO:2704 is the determined cDNA sequence of clone 61814436
SEQ ID NO:2705 is the determined cDNA sequence of clone 61814437
20 SEQ ID NO:2706 is the determined cDNA sequence of clone 61814438
SEQ ID NO:2707 is the determined cDNA sequence of clone 61814439
SEQ ID NO:2708 is the determined cDNA sequence of clone 61814440
SEQ ID NO:2709 is the determined cDNA sequence of clone 61814441
SEQ ID NO:2710 is the determined cDNA sequence of clone 61814442
25 SEQ ID NO:2711 is the determined cDNA sequence of clone 61814443
SEQ ID NO:2712 is the determined cDNA sequence of clone 61814444
SEQ ID NO:2713 is the determined cDNA sequence of clone 61814445
SEQ ID NO:2714 is the determined cDNA sequence of clone 61814446
SEQ ID NO:2715 is the determined cDNA sequence of clone 61814447
30 SEQ ID NO:2716 is the determined cDNA sequence of clone 61823768
SEQ ID NO:2717 is the determined cDNA sequence of clone 61823769

SEQ ID NO:2718 is the determined cDNA sequence of clone 61823770
SEQ ID NO:2719 is the determined cDNA sequence of clone 61823772
SEQ ID NO:2720 is the determined cDNA sequence of clone 61823773
SEQ ID NO:2721 is the determined cDNA sequence of clone 61823774
5 SEQ ID NO:2722 is the determined cDNA sequence of clone 61823775
SEQ ID NO:2723 is the determined cDNA sequence of clone 61823777
SEQ ID NO:2724 is the determined cDNA sequence of clone 61823778
SEQ ID NO:2725 is the determined cDNA sequence of clone 61823779
SEQ ID NO:2726 is the determined cDNA sequence of clone 61823780
10 SEQ ID NO:2727 is the determined cDNA sequence of clone 61823781
SEQ ID NO:2728 is the determined cDNA sequence of clone 61823782
SEQ ID NO:2729 is the determined cDNA sequence of clone 61823784
SEQ ID NO:2730 is the determined cDNA sequence of clone 61823785
SEQ ID NO:2731 is the determined cDNA sequence of clone 61823786
15 SEQ ID NO:2732 is the determined cDNA sequence of clone 61823787
SEQ ID NO:2733 is the determined cDNA sequence of clone 61823788
SEQ ID NO:2734 is the determined cDNA sequence of clone 61823789
SEQ ID NO:2735 is the determined cDNA sequence of clone 61823790
SEQ ID NO:2736 is the determined cDNA sequence of clone 61823791
20 SEQ ID NO:2737 is the determined cDNA sequence of clone 61823792
SEQ ID NO:2738 is the determined cDNA sequence of clone 61823793
SEQ ID NO:2739 is the determined cDNA sequence of clone 61823794
SEQ ID NO:2740 is the determined cDNA sequence of clone 61823797
SEQ ID NO:2741 is the determined cDNA sequence of clone 61823798
25 SEQ ID NO:2742 is the determined cDNA sequence of clone 61823799
SEQ ID NO:2743 is the determined cDNA sequence of clone 61823800
SEQ ID NO:2744 is the determined cDNA sequence of clone 61823801
SEQ ID NO:2745 is the determined cDNA sequence of clone 61823802
SEQ ID NO:2746 is the determined cDNA sequence of clone 61823803
30 SEQ ID NO:2747 is the determined cDNA sequence of clone 61823804
SEQ ID NO:2748 is the determined cDNA sequence of clone 61823805

SEQ ID NO:2749 is the determined cDNA sequence of clone 61823807
SEQ ID NO:2750 is the determined cDNA sequence of clone 61823808
SEQ ID NO:2751 is the determined cDNA sequence of clone 61823809
SEQ ID NO:2752 is the determined cDNA sequence of clone 61823810
5 SEQ ID NO:2753 is the determined cDNA sequence of clone 61823811
SEQ ID NO:2754 is the determined cDNA sequence of clone 61823812
SEQ ID NO:2755 is the determined cDNA sequence of clone 61823813
SEQ ID NO:2756 is the determined cDNA sequence of clone 61823814
SEQ ID NO:2757 is the determined cDNA sequence of clone 61823815
10 SEQ ID NO:2758 is the determined cDNA sequence of clone 61823816
SEQ ID NO:2759 is the determined cDNA sequence of clone 61823817
SEQ ID NO:2760 is the determined cDNA sequence of clone 61823818
SEQ ID NO:2761 is the determined cDNA sequence of clone 61823820
SEQ ID NO:2762 is the determined cDNA sequence of clone 61823821
15 SEQ ID NO:2763 is the determined cDNA sequence of clone 61823822
SEQ ID NO:2764 is the determined cDNA sequence of clone 61823823
SEQ ID NO:2765 is the determined cDNA sequence of clone 61823824
SEQ ID NO:2766 is the determined cDNA sequence of clone 61823825
SEQ ID NO:2767 is the determined cDNA sequence of clone 61823826
20 SEQ ID NO:2768 is the determined cDNA sequence of clone 61823827
SEQ ID NO:2769 is the determined cDNA sequence of clone 61823829
SEQ ID NO:2770 is the determined cDNA sequence of clone 61823830
SEQ ID NO:2771 is the determined cDNA sequence of clone 61823831
SEQ ID NO:2772 is the determined cDNA sequence of clone 61823833
25 SEQ ID NO:2773 is the determined cDNA sequence of clone 61823835
SEQ ID NO:2774 is the determined cDNA sequence of clone 61823837
SEQ ID NO:2775 is the determined cDNA sequence of clone 61823839
SEQ ID NO:2776 is the determined cDNA sequence of clone 61823840
SEQ ID NO:2777 is the determined cDNA sequence of clone 61823841
30 SEQ ID NO:2778 is the determined cDNA sequence of clone 61823843
SEQ ID NO:2779 is the determined cDNA sequence of clone 61823844

SEQ ID NO:2780 is the determined cDNA sequence of clone 61823845
SEQ ID NO:2781 is the determined cDNA sequence of clone 61823847
SEQ ID NO:2782 is the determined cDNA sequence of clone 61823849
SEQ ID NO:2783 is the determined cDNA sequence of clone 61823850
5 SEQ ID NO:2784 is the determined cDNA sequence of clone 61823851
SEQ ID NO:2785 is the determined cDNA sequence of clone 61823852
SEQ ID NO:2786 is the determined cDNA sequence of clone 61823854
SEQ ID NO:2787 is the determined cDNA sequence of clone 61823855
SEQ ID NO:2788 is the determined cDNA sequence of clone 61823856
10 SEQ ID NO:2789 is the determined cDNA sequence of clone 61823858
SEQ ID NO:2790 is the determined cDNA sequence of clone 61823859
SEQ ID NO:2791 is the determined cDNA sequence of clone 62342414
SEQ ID NO:2792 is the determined cDNA sequence of clone 62342416
SEQ ID NO:2793 is the determined cDNA sequence of clone 62342417
15 SEQ ID NO:2794 is the determined cDNA sequence of clone 62342422
SEQ ID NO:2795 is the determined cDNA sequence of clone 62342423
SEQ ID NO:2796 is the determined cDNA sequence of clone 62342425
SEQ ID NO:2797 is the determined cDNA sequence of clone 62342426
SEQ ID NO:2798 is the determined cDNA sequence of clone 62342428
20 SEQ ID NO:2799 is the determined cDNA sequence of clone 62342429
SEQ ID NO:2800 is the determined cDNA sequence of clone 62342430
SEQ ID NO:2801 is the determined cDNA sequence of clone 62342433
SEQ ID NO:2802 is the determined cDNA sequence of clone 62342434
SEQ ID NO:2803 is the determined cDNA sequence of clone 62342436
25 SEQ ID NO:2804 is the determined cDNA sequence of clone 62342437
SEQ ID NO:2805 is the determined cDNA sequence of clone 62342438
SEQ ID NO:2806 is the determined cDNA sequence of clone 62342439
SEQ ID NO:2807 is the determined cDNA sequence of clone 62342440
SEQ ID NO:2808 is the determined cDNA sequence of clone 62342442
30 SEQ ID NO:2809 is the determined cDNA sequence of clone 62342443
SEQ ID NO:2810 is the determined cDNA sequence of clone 62342447

SEQ ID NO:2811 is the determined cDNA sequence of clone 62342449
SEQ ID NO:2812 is the determined cDNA sequence of clone 62342452
SEQ ID NO:2813 is the determined cDNA sequence of clone 62342453
SEQ ID NO:2814 is the determined cDNA sequence of clone 62342454
5 SEQ ID NO:2815 is the determined cDNA sequence of clone 62342455
SEQ ID NO:2816 is the determined cDNA sequence of clone 62342456
SEQ ID NO:2817 is the determined cDNA sequence of clone 62342457
SEQ ID NO:2818 is the determined cDNA sequence of clone 62342458
SEQ ID NO:2819 is the determined cDNA sequence of clone 62342460
10 SEQ ID NO:2820 is the determined cDNA sequence of clone 62342462
SEQ ID NO:2821 is the determined cDNA sequence of clone 62342464
SEQ ID NO:2822 is the determined cDNA sequence of clone 62342467
SEQ ID NO:2823 is the determined cDNA sequence of clone 62342468
SEQ ID NO:2824 is the determined cDNA sequence of clone 62342469
15 SEQ ID NO:2825 is the determined cDNA sequence of clone 62342471
SEQ ID NO:2826 is the determined cDNA sequence of clone 62342476
SEQ ID NO:2827 is the determined cDNA sequence of clone 62342477
SEQ ID NO:2828 is the determined cDNA sequence of clone 62342480
SEQ ID NO:2829 is the determined cDNA sequence of clone 62342481
20 SEQ ID NO:2830 is the determined cDNA sequence of clone 62342484
SEQ ID NO:2831 is the determined cDNA sequence of clone 62342485
SEQ ID NO:2832 is the determined cDNA sequence of clone 62342488
SEQ ID NO:2833 is the determined cDNA sequence of clone 62342489
SEQ ID NO:2834 is the determined cDNA sequence of clone 62342490
25 SEQ ID NO:2835 is the determined cDNA sequence of clone 62342492
SEQ ID NO:2836 is the determined cDNA sequence of clone 62342493
SEQ ID NO:2837 is the determined cDNA sequence of clone 62342495
SEQ ID NO:2838 is the determined cDNA sequence of clone 62342497
SEQ ID NO:2839 is the determined cDNA sequence of clone 62342498
30 SEQ ID NO:2840 is the determined cDNA sequence of clone 62342504
SEQ ID NO:2841 is the determined cDNA sequence of clone 61814542

SEQ ID NO:2842 is the determined cDNA sequence of clone 61814543
SEQ ID NO:2843 is the determined cDNA sequence of clone 61814546
SEQ ID NO:2844 is the determined cDNA sequence of clone 61814548
SEQ ID NO:2845 is the determined cDNA sequence of clone 61814549
5 SEQ ID NO:2846 is the determined cDNA sequence of clone 61814550
SEQ ID NO:2847 is the determined cDNA sequence of clone 61814551
SEQ ID NO:2848 is the determined cDNA sequence of clone 61814552
SEQ ID NO:2849 is the determined cDNA sequence of clone 61814553
SEQ ID NO:2850 is the determined cDNA sequence of clone 61814554
10 SEQ ID NO:2851 is the determined cDNA sequence of clone 61814555
SEQ ID NO:2852 is the determined cDNA sequence of clone 61814556
SEQ ID NO:2853 is the determined cDNA sequence of clone 61814561
SEQ ID NO:2854 is the determined cDNA sequence of clone 61814562
SEQ ID NO:2855 is the determined cDNA sequence of clone 61814566
15 SEQ ID NO:2856 is the determined cDNA sequence of clone 61814568
SEQ ID NO:2857 is the determined cDNA sequence of clone 61814569
SEQ ID NO:2858 is the determined cDNA sequence of clone 61814570
SEQ ID NO:2859 is the determined cDNA sequence of clone 61814571
SEQ ID NO:2860 is the determined cDNA sequence of clone 61814572
20 SEQ ID NO:2861 is the determined cDNA sequence of clone 61814573
SEQ ID NO:2862 is the determined cDNA sequence of clone 61814575
SEQ ID NO:2863 is the determined cDNA sequence of clone 61814576
SEQ ID NO:2864 is the determined cDNA sequence of clone 61814577
SEQ ID NO:2865 is the determined cDNA sequence of clone 61814579
25 SEQ ID NO:2866 is the determined cDNA sequence of clone 61814580
SEQ ID NO:2867 is the determined cDNA sequence of clone 61814581
SEQ ID NO:2868 is the determined cDNA sequence of clone 61814583
SEQ ID NO:2869 is the determined cDNA sequence of clone 61814584
SEQ ID NO:2870 is the determined cDNA sequence of clone 61814585
30 SEQ ID NO:2871 is the determined cDNA sequence of clone 61814586
SEQ ID NO:2872 is the determined cDNA sequence of clone 61814587

SEQ ID NO:2873 is the determined cDNA sequence of clone 61814588
SEQ ID NO:2874 is the determined cDNA sequence of clone 61814589
SEQ ID NO:2875 is the determined cDNA sequence of clone 61814590
SEQ ID NO:2876 is the determined cDNA sequence of clone 61814591
5 SEQ ID NO:2877 is the determined cDNA sequence of clone 61814592
SEQ ID NO:2878 is the determined cDNA sequence of clone 61814595
SEQ ID NO:2879 is the determined cDNA sequence of clone 61814596
SEQ ID NO:2880 is the determined cDNA sequence of clone 61814598
SEQ ID NO:2881 is the determined cDNA sequence of clone 61814600
10 SEQ ID NO:2882 is the determined cDNA sequence of clone 61814601
SEQ ID NO:2883 is the determined cDNA sequence of clone 61814602
SEQ ID NO:2884 is the determined cDNA sequence of clone 61814604
SEQ ID NO:2885 is the determined cDNA sequence of clone 61814605
SEQ ID NO:2886 is the determined cDNA sequence of clone 61814606
15 SEQ ID NO:2887 is the determined cDNA sequence of clone 61814607
SEQ ID NO:2888 is the determined cDNA sequence of clone 61814608
SEQ ID NO:2889 is the determined cDNA sequence of clone 61814609
SEQ ID NO:2890 is the determined cDNA sequence of clone 61814610
SEQ ID NO:2891 is the determined cDNA sequence of clone 61814611
20 SEQ ID NO:2892 is the determined cDNA sequence of clone 61814612
SEQ ID NO:2893 is the determined cDNA sequence of clone 61814613
SEQ ID NO:2894 is the determined cDNA sequence of clone 61814614
SEQ ID NO:2895 is the determined cDNA sequence of clone 61814615
SEQ ID NO:2896 is the determined cDNA sequence of clone 61814616
25 SEQ ID NO:2897 is the determined cDNA sequence of clone 61814617
SEQ ID NO:2898 is the determined cDNA sequence of clone 61814618
SEQ ID NO:2899 is the determined cDNA sequence of clone 61814619
SEQ ID NO:2900 is the determined cDNA sequence of clone 61814620
SEQ ID NO:2901 is the determined cDNA sequence of clone 61814622
30 SEQ ID NO:2902 is the determined cDNA sequence of clone 61814623
SEQ ID NO:2903 is the determined cDNA sequence of clone 61814624

SEQ ID NO:2904 is the determined cDNA sequence of clone 61814625
SEQ ID NO:2905 is the determined cDNA sequence of clone 61814626
SEQ ID NO:2906 is the determined cDNA sequence of clone 61814627
SEQ ID NO:2907 is the determined cDNA sequence of clone 61814628
5 SEQ ID NO:2908 is the determined cDNA sequence of clone 61814629
SEQ ID NO:2909 is the determined cDNA sequence of clone 61814630
SEQ ID NO:2910 is the determined cDNA sequence of clone 61814631
SEQ ID NO:2911 is the determined cDNA sequence of clone 61814633
SEQ ID NO:2912 is the determined cDNA sequence of clone 61814449
10 SEQ ID NO:2913 is the determined cDNA sequence of clone 61814450
SEQ ID NO:2914 is the determined cDNA sequence of clone 61814452
SEQ ID NO:2915 is the determined cDNA sequence of clone 61814453
SEQ ID NO:2916 is the determined cDNA sequence of clone 61814454
SEQ ID NO:2917 is the determined cDNA sequence of clone 61814456
15 SEQ ID NO:2918 is the determined cDNA sequence of clone 61814457
SEQ ID NO:2919 is the determined cDNA sequence of clone 61814458
SEQ ID NO:2920 is the determined cDNA sequence of clone 61814459
SEQ ID NO:2921 is the determined cDNA sequence of clone 61814460
SEQ ID NO:2922 is the determined cDNA sequence of clone 61814461
20 SEQ ID NO:2923 is the determined cDNA sequence of clone 61814462
SEQ ID NO:2924 is the determined cDNA sequence of clone 61814466
SEQ ID NO:2925 is the determined cDNA sequence of clone 61814467
SEQ ID NO:2926 is the determined cDNA sequence of clone 61814468
SEQ ID NO:2927 is the determined cDNA sequence of clone 61814470
25 SEQ ID NO:2928 is the determined cDNA sequence of clone 61814471
SEQ ID NO:2929 is the determined cDNA sequence of clone 61814472
SEQ ID NO:2930 is the determined cDNA sequence of clone 61814473
SEQ ID NO:2931 is the determined cDNA sequence of clone 61814474
SEQ ID NO:2932 is the determined cDNA sequence of clone 61814476
30 SEQ ID NO:2933 is the determined cDNA sequence of clone 61814478
SEQ ID NO:2934 is the determined cDNA sequence of clone 61814483

SEQ ID NO:2935 is the determined cDNA sequence of clone 61814484
SEQ ID NO:2936 is the determined cDNA sequence of clone 61814485
SEQ ID NO:2937 is the determined cDNA sequence of clone 61814486
SEQ ID NO:2938 is the determined cDNA sequence of clone 61814487
5 SEQ ID NO:2939 is the determined cDNA sequence of clone 61814489
SEQ ID NO:2940 is the determined cDNA sequence of clone 61814490
SEQ ID NO:2941 is the determined cDNA sequence of clone 61814492
SEQ ID NO:2942 is the determined cDNA sequence of clone 61814494
SEQ ID NO:2943 is the determined cDNA sequence of clone 61814495
10 SEQ ID NO:2944 is the determined cDNA sequence of clone 61814496
SEQ ID NO:2945 is the determined cDNA sequence of clone 61814497
SEQ ID NO:2946 is the determined cDNA sequence of clone 61814498
SEQ ID NO:2947 is the determined cDNA sequence of clone 61814499
SEQ ID NO:2948 is the determined cDNA sequence of clone 61814500
15 SEQ ID NO:2949 is the determined cDNA sequence of clone 61814502
SEQ ID NO:2950 is the determined cDNA sequence of clone 61814503
SEQ ID NO:2951 is the determined cDNA sequence of clone 61814505
SEQ ID NO:2952 is the determined cDNA sequence of clone 61814506
SEQ ID NO:2953 is the determined cDNA sequence of clone 61814508
20 SEQ ID NO:2954 is the determined cDNA sequence of clone 61814509
SEQ ID NO:2955 is the determined cDNA sequence of clone 61814510
SEQ ID NO:2956 is the determined cDNA sequence of clone 61814512
SEQ ID NO:2957 is the determined cDNA sequence of clone 61814513
SEQ ID NO:2958 is the determined cDNA sequence of clone 61814514
25 SEQ ID NO:2959 is the determined cDNA sequence of clone 61814517
SEQ ID NO:2960 is the determined cDNA sequence of clone 61814518
SEQ ID NO:2961 is the determined cDNA sequence of clone 61814520
SEQ ID NO:2962 is the determined cDNA sequence of clone 61814521
SEQ ID NO:2963 is the determined cDNA sequence of clone 61814522
30 SEQ ID NO:2964 is the determined cDNA sequence of clone 61814523
SEQ ID NO:2965 is the determined cDNA sequence of clone 61814524

SEQ ID NO:2966 is the determined cDNA sequence of clone 61814525
SEQ ID NO:2967 is the determined cDNA sequence of clone 61814526
SEQ ID NO:2968 is the determined cDNA sequence of clone 61814528
SEQ ID NO:2969 is the determined cDNA sequence of clone 61814530
5 SEQ ID NO:2970 is the determined cDNA sequence of clone 61814531
SEQ ID NO:2971 is the determined cDNA sequence of clone 61814532
SEQ ID NO:2972 is the determined cDNA sequence of clone 61814534
SEQ ID NO:2973 is the determined cDNA sequence of clone 61814535
SEQ ID NO:2974 is the determined cDNA sequence of clone 61814536
10 SEQ ID NO:2975 is the determined cDNA sequence of clone 61814537
SEQ ID NO:2976 is the determined cDNA sequence of clone 61814538
SEQ ID NO:2977 is the determined cDNA sequence of clone 61814539
SEQ ID NO:2978 is the determined cDNA sequence of clone 61814540
SEQ ID NO:2979 is the determined cDNA sequence of clone 62210387
15 SEQ ID NO:2980 is the determined cDNA sequence of clone 62210388
SEQ ID NO:2981 is the determined cDNA sequence of clone 62210389
SEQ ID NO:2982 is the determined cDNA sequence of clone 62210390
SEQ ID NO:2983 is the determined cDNA sequence of clone 62210391
SEQ ID NO:2984 is the determined cDNA sequence of clone 62210394
20 SEQ ID NO:2985 is the determined cDNA sequence of clone 62210395
SEQ ID NO:2986 is the determined cDNA sequence of clone 62210397
SEQ ID NO:2987 is the determined cDNA sequence of clone 62210398
SEQ ID NO:2988 is the determined cDNA sequence of clone 62210399
SEQ ID NO:2989 is the determined cDNA sequence of clone 62210401
25 SEQ ID NO:2990 is the determined cDNA sequence of clone 62210403
SEQ ID NO:2991 is the determined cDNA sequence of clone 62210404
SEQ ID NO:2992 is the determined cDNA sequence of clone 63231658
SEQ ID NO:2993 is the determined cDNA sequence of clone 63231659
SEQ ID NO:2994 is the determined cDNA sequence of clone 63231660
30 SEQ ID NO:2995 is the determined cDNA sequence of clone 63231661
SEQ ID NO:2996 is the determined cDNA sequence of clone 63231662

SEQ ID NO:2997 is the determined cDNA sequence of clone 63231664
SEQ ID NO:2998 is the determined cDNA sequence of clone 63231665
SEQ ID NO:2999 is the determined cDNA sequence of clone 63231666
SEQ ID NO:3000 is the determined cDNA sequence of clone 63231667
5 SEQ ID NO:3001 is the determined cDNA sequence of clone 63231668
SEQ ID NO:3002 is the determined cDNA sequence of clone 63231669
SEQ ID NO:3003 is the determined cDNA sequence of clone 63231670
SEQ ID NO:3004 is the determined cDNA sequence of clone 63231671
SEQ ID NO:3005 is the determined cDNA sequence of clone 63231672
10 SEQ ID NO:3006 is the determined cDNA sequence of clone 63231673
SEQ ID NO:3007 is the determined cDNA sequence of clone 63231674
SEQ ID NO:3008 is the determined cDNA sequence of clone 63231675
SEQ ID NO:3009 is the determined cDNA sequence of clone 63231676
SEQ ID NO:3010 is the determined cDNA sequence of clone 63231677
15 SEQ ID NO:3011 is the determined cDNA sequence of clone 63231678
SEQ ID NO:3012 is the determined cDNA sequence of clone 63231679
SEQ ID NO:3013 is the determined cDNA sequence of clone 63231680
SEQ ID NO:3014 is the determined cDNA sequence of clone 63231681
SEQ ID NO:3015 is the determined cDNA sequence of clone 63231682
20 SEQ ID NO:3016 is the determined cDNA sequence of clone 63231683
SEQ ID NO:3017 is the determined cDNA sequence of clone 63231684
SEQ ID NO:3018 is the determined cDNA sequence of clone 63231685
SEQ ID NO:3019 is the determined cDNA sequence of clone 63231686
SEQ ID NO:3020 is the determined cDNA sequence of clone 63231687
25 SEQ ID NO:3021 is the determined cDNA sequence of clone 63231688
SEQ ID NO:3022 is the determined cDNA sequence of clone 63231689
SEQ ID NO:3023 is the determined cDNA sequence of clone 63231690
SEQ ID NO:3024 is the determined cDNA sequence of clone 63231691
SEQ ID NO:3025 is the determined cDNA sequence of clone 63231692
30 SEQ ID NO:3026 is the determined cDNA sequence of clone 63231693
SEQ ID NO:3027 is the determined cDNA sequence of clone 63231694

SEQ ID NO:3028 is the determined cDNA sequence of clone 63231695
SEQ ID NO:3029 is the determined cDNA sequence of clone 63231696
SEQ ID NO:3030 is the determined cDNA sequence of clone 63231697
SEQ ID NO:3031 is the determined cDNA sequence of clone 63231698
5 SEQ ID NO:3032 is the determined cDNA sequence of clone 63231699
SEQ ID NO:3033 is the determined cDNA sequence of clone 63231700
SEQ ID NO:3034 is the determined cDNA sequence of clone 63231701
SEQ ID NO:3035 is the determined cDNA sequence of clone 63231702
SEQ ID NO:3036 is the determined cDNA sequence of clone 63231703
10 SEQ ID NO:3037 is the determined cDNA sequence of clone 63231704
SEQ ID NO:3038 is the determined cDNA sequence of clone 63231705
SEQ ID NO:3039 is the determined cDNA sequence of clone 63231706
SEQ ID NO:3040 is the determined cDNA sequence of clone 63231707
SEQ ID NO:3041 is the determined cDNA sequence of clone 63231708
15 SEQ ID NO:3042 is the determined cDNA sequence of clone 63231709
SEQ ID NO:3043 is the determined cDNA sequence of clone 63231711
SEQ ID NO:3044 is the determined cDNA sequence of clone 63231713
SEQ ID NO:3045 is the determined cDNA sequence of clone 63231715
SEQ ID NO:3046 is the determined cDNA sequence of clone 63231716
20 SEQ ID NO:3047 is the determined cDNA sequence of clone 63231717
SEQ ID NO:3048 is the determined cDNA sequence of clone 63231718
SEQ ID NO:3049 is the determined cDNA sequence of clone 63231719
SEQ ID NO:3050 is the determined cDNA sequence of clone 63231720
SEQ ID NO:3051 is the determined cDNA sequence of clone 63231721
25 SEQ ID NO:3052 is the determined cDNA sequence of clone 63231723
SEQ ID NO:3053 is the determined cDNA sequence of clone 63231724
SEQ ID NO:3054 is the determined cDNA sequence of clone 63231725
SEQ ID NO:3055 is the determined cDNA sequence of clone 63231726
SEQ ID NO:3056 is the determined cDNA sequence of clone 63231727
30 SEQ ID NO:3057 is the determined cDNA sequence of clone 63231729
SEQ ID NO:3058 is the determined cDNA sequence of clone 63231730

SEQ ID NO:3059 is the determined cDNA sequence of clone 63231731
SEQ ID NO:3060 is the determined cDNA sequence of clone 63231732
SEQ ID NO:3061 is the determined cDNA sequence of clone 63138223
SEQ ID NO:3062 is the determined cDNA sequence of clone 63138224
5 SEQ ID NO:3063 is the determined cDNA sequence of clone 63138225
SEQ ID NO:3064 is the determined cDNA sequence of clone 63138226
SEQ ID NO:3065 is the determined cDNA sequence of clone 63138227
SEQ ID NO:3066 is the determined cDNA sequence of clone 63138228
SEQ ID NO:3067 is the determined cDNA sequence of clone 63138229
10 SEQ ID NO:3068 is the determined cDNA sequence of clone 63138230
SEQ ID NO:3069 is the determined cDNA sequence of clone 63138231
SEQ ID NO:3070 is the determined cDNA sequence of clone 63138232
SEQ ID NO:3071 is the determined cDNA sequence of clone 63138233
SEQ ID NO:3072 is the determined cDNA sequence of clone 63138234
15 SEQ ID NO:3073 is the determined cDNA sequence of clone 63138235
SEQ ID NO:3074 is the determined cDNA sequence of clone 63138237
SEQ ID NO:3075 is the determined cDNA sequence of clone 63138239
SEQ ID NO:3076 is the determined cDNA sequence of clone 63138240
SEQ ID NO:3077 is the determined cDNA sequence of clone 63138241
20 SEQ ID NO:3078 is the determined cDNA sequence of clone 63138242
SEQ ID NO:3079 is the determined cDNA sequence of clone 63138243
SEQ ID NO:3080 is the determined cDNA sequence of clone 63138244
SEQ ID NO:3081 is the determined cDNA sequence of clone 63138246
SEQ ID NO:3082 is the determined cDNA sequence of clone 63138249
25 SEQ ID NO:3083 is the determined cDNA sequence of clone 63138250
SEQ ID NO:3084 is the determined cDNA sequence of clone 63138251
SEQ ID NO:3085 is the determined cDNA sequence of clone 63138252
SEQ ID NO:3086 is the determined cDNA sequence of clone 63138253
SEQ ID NO:3087 is the determined cDNA sequence of clone 63138254
30 SEQ ID NO:3088 is the determined cDNA sequence of clone 63138255
SEQ ID NO:3089 is the determined cDNA sequence of clone 63138256

SEQ ID NO:3090 is the determined cDNA sequence of clone 63138257
SEQ ID NO:3091 is the determined cDNA sequence of clone 63138258
SEQ ID NO:3092 is the determined cDNA sequence of clone 63138259
SEQ ID NO:3093 is the determined cDNA sequence of clone 63138260
5 SEQ ID NO:3094 is the determined cDNA sequence of clone 63138262
SEQ ID NO:3095 is the determined cDNA sequence of clone 63138264
SEQ ID NO:3096 is the determined cDNA sequence of clone 63138265
SEQ ID NO:3097 is the determined cDNA sequence of clone 63138266
SEQ ID NO:3098 is the determined cDNA sequence of clone 63138267
10 SEQ ID NO:3099 is the determined cDNA sequence of clone 63138268
SEQ ID NO:3100 is the determined cDNA sequence of clone 63138269
SEQ ID NO:3101 is the determined cDNA sequence of clone 63138270
SEQ ID NO:3102 is the determined cDNA sequence of clone 63138271
SEQ ID NO:3103 is the determined cDNA sequence of clone 63138272
15 SEQ ID NO:3104 is the determined cDNA sequence of clone 63138273
SEQ ID NO:3105 is the determined cDNA sequence of clone 63138274
SEQ ID NO:3106 is the determined cDNA sequence of clone 63138275
SEQ ID NO:3107 is the determined cDNA sequence of clone 63138276
SEQ ID NO:3108 is the determined cDNA sequence of clone 63138277
20 SEQ ID NO:3109 is the determined cDNA sequence of clone 63138278
SEQ ID NO:3110 is the determined cDNA sequence of clone 63138279
SEQ ID NO:3111 is the determined cDNA sequence of clone 63138280
SEQ ID NO:3112 is the determined cDNA sequence of clone 63138281
SEQ ID NO:3113 is the determined cDNA sequence of clone 63138282
25 SEQ ID NO:3114 is the determined cDNA sequence of clone 63138283
SEQ ID NO:3115 is the determined cDNA sequence of clone 63138284
SEQ ID NO:3116 is the determined cDNA sequence of clone 63138285
SEQ ID NO:3117 is the determined cDNA sequence of clone 63138286
SEQ ID NO:3118 is the determined cDNA sequence of clone 63138287
30 SEQ ID NO:3119 is the determined cDNA sequence of clone 63138288
SEQ ID NO:3120 is the determined cDNA sequence of clone 63138289

SEQ ID NO:3121 is the determined cDNA sequence of clone 63138290
SEQ ID NO:3122 is the determined cDNA sequence of clone 63138291
SEQ ID NO:3123 is the determined cDNA sequence of clone 63138292
SEQ ID NO:3124 is the determined cDNA sequence of clone 63138294
5 SEQ ID NO:3125 is the determined cDNA sequence of clone 63138295
SEQ ID NO:3126 is the determined cDNA sequence of clone 63138296
SEQ ID NO:3127 is the determined cDNA sequence of clone 63138297
SEQ ID NO:3128 is the determined cDNA sequence of clone 63138298
SEQ ID NO:3129 is the determined cDNA sequence of clone 63138299
10 SEQ ID NO:3130 is the determined cDNA sequence of clone 63138300
SEQ ID NO:3131 is the determined cDNA sequence of clone 63138302
SEQ ID NO:3132 is the determined cDNA sequence of clone 63138303
SEQ ID NO:3133 is the determined cDNA sequence of clone 63138304
SEQ ID NO:3134 is the determined cDNA sequence of clone 63138305
15 SEQ ID NO:3135 is the determined cDNA sequence of clone 63138306
SEQ ID NO:3136 is the determined cDNA sequence of clone 63138308
SEQ ID NO:3137 is the determined cDNA sequence of clone 63138309
SEQ ID NO:3138 is the determined cDNA sequence of clone 63138311
SEQ ID NO:3139 is the determined cDNA sequence of clone 63138312
20 SEQ ID NO:3140 is the determined cDNA sequence of clone 63138313
SEQ ID NO:3141 is the determined cDNA sequence of clone 63138314
SEQ ID NO:3142 is the determined cDNA sequence of clone 63298516
SEQ ID NO:3143 is the determined cDNA sequence of clone 63298517
SEQ ID NO:3144 is the determined cDNA sequence of clone 63298518
25 SEQ ID NO:3145 is the determined cDNA sequence of clone 63298519
SEQ ID NO:3146 is the determined cDNA sequence of clone 63298520
SEQ ID NO:3147 is the determined cDNA sequence of clone 63298521
SEQ ID NO:3148 is the determined cDNA sequence of clone 63298522
SEQ ID NO:3149 is the determined cDNA sequence of clone 63298523
30 SEQ ID NO:3150 is the determined cDNA sequence of clone 63298524
SEQ ID NO:3151 is the determined cDNA sequence of clone 63298526

SEQ ID NO:3152 is the determined cDNA sequence of clone 63298527
SEQ ID NO:3153 is the determined cDNA sequence of clone 63298528
SEQ ID NO:3154 is the determined cDNA sequence of clone 63298529
SEQ ID NO:3155 is the determined cDNA sequence of clone 63298530
5 SEQ ID NO:3156 is the determined cDNA sequence of clone 63298531
SEQ ID NO:3157 is the determined cDNA sequence of clone 63298532
SEQ ID NO:3158 is the determined cDNA sequence of clone 63298533
SEQ ID NO:3159 is the determined cDNA sequence of clone 63298534
SEQ ID NO:3160 is the determined cDNA sequence of clone 63298535
10 SEQ ID NO:3161 is the determined cDNA sequence of clone 63298537
SEQ ID NO:3162 is the determined cDNA sequence of clone 63298538
SEQ ID NO:3163 is the determined cDNA sequence of clone 63298539
SEQ ID NO:3164 is the determined cDNA sequence of clone 63298540
SEQ ID NO:3165 is the determined cDNA sequence of clone 63298541
15 SEQ ID NO:3166 is the determined cDNA sequence of clone 63298542
SEQ ID NO:3167 is the determined cDNA sequence of clone 63298543
SEQ ID NO:3168 is the determined cDNA sequence of clone 63298544
SEQ ID NO:3169 is the determined cDNA sequence of clone 63298545
SEQ ID NO:3170 is the determined cDNA sequence of clone 63298546
20 SEQ ID NO:3171 is the determined cDNA sequence of clone 63298547
SEQ ID NO:3172 is the determined cDNA sequence of clone 63298548
SEQ ID NO:3173 is the determined cDNA sequence of clone 63298549
SEQ ID NO:3174 is the determined cDNA sequence of clone 63298550
SEQ ID NO:3175 is the determined cDNA sequence of clone 63298551
25 SEQ ID NO:3176 is the determined cDNA sequence of clone 63298552
SEQ ID NO:3177 is the determined cDNA sequence of clone 63298554
SEQ ID NO:3178 is the determined cDNA sequence of clone 63298555
SEQ ID NO:3179 is the determined cDNA sequence of clone 63298556
SEQ ID NO:3180 is the determined cDNA sequence of clone 63298557
30 SEQ ID NO:3181 is the determined cDNA sequence of clone 63298558
SEQ ID NO:3182 is the determined cDNA sequence of clone 63298559

SEQ ID NO:3183 is the determined cDNA sequence of clone 63298560
SEQ ID NO:3184 is the determined cDNA sequence of clone 63298561
SEQ ID NO:3185 is the determined cDNA sequence of clone 63298562
SEQ ID NO:3186 is the determined cDNA sequence of clone 63298563
5 SEQ ID NO:3187 is the determined cDNA sequence of clone 63298564
SEQ ID NO:3188 is the determined cDNA sequence of clone 63298565
SEQ ID NO:3189 is the determined cDNA sequence of clone 63298566
SEQ ID NO:3190 is the determined cDNA sequence of clone 63298567
SEQ ID NO:3191 is the determined cDNA sequence of clone 63298568
10 SEQ ID NO:3192 is the determined cDNA sequence of clone 63298569
SEQ ID NO:3193 is the determined cDNA sequence of clone 63298570
SEQ ID NO:3194 is the determined cDNA sequence of clone 63298571
SEQ ID NO:3195 is the determined cDNA sequence of clone 63298572
SEQ ID NO:3196 is the determined cDNA sequence of clone 63298573
15 SEQ ID NO:3197 is the determined cDNA sequence of clone 63298574
SEQ ID NO:3198 is the determined cDNA sequence of clone 63298575
SEQ ID NO:3199 is the determined cDNA sequence of clone 63298576
SEQ ID NO:3200 is the determined cDNA sequence of clone 63298577
SEQ ID NO:3201 is the determined cDNA sequence of clone 63298579
20 SEQ ID NO:3202 is the determined cDNA sequence of clone 63298580
SEQ ID NO:3203 is the determined cDNA sequence of clone 63298581
SEQ ID NO:3204 is the determined cDNA sequence of clone 63298582
SEQ ID NO:3205 is the determined cDNA sequence of clone 63298583
SEQ ID NO:3206 is the determined cDNA sequence of clone 63298584
25 SEQ ID NO:3207 is the determined cDNA sequence of clone 63298585
SEQ ID NO:3208 is the determined cDNA sequence of clone 63298586
SEQ ID NO:3209 is the determined cDNA sequence of clone 63298588
SEQ ID NO:3210 is the determined cDNA sequence of clone 63298589
SEQ ID NO:3211 is the determined cDNA sequence of clone 63298590
30 SEQ ID NO:3212 is the determined cDNA sequence of clone 63298591
SEQ ID NO:3213 is the determined cDNA sequence of clone 63298592

SEQ ID NO:3214 is the determined cDNA sequence of clone 63298593
SEQ ID NO:3215 is the determined cDNA sequence of clone 63298594
SEQ ID NO:3216 is the determined cDNA sequence of clone 63298595
SEQ ID NO:3217 is the determined cDNA sequence of clone 63298596
5 SEQ ID NO:3218 is the determined cDNA sequence of clone 63298597
SEQ ID NO:3219 is the determined cDNA sequence of clone 63298599
SEQ ID NO:3220 is the determined cDNA sequence of clone 63298600
SEQ ID NO:3221 is the determined cDNA sequence of clone 63298601
SEQ ID NO:3222 is the determined cDNA sequence of clone 63298602
10 SEQ ID NO:3223 is the determined cDNA sequence of clone 63298603
SEQ ID NO:3224 is the determined cDNA sequence of clone 63298604
SEQ ID NO:3225 is the determined cDNA sequence of clone 63298605
SEQ ID NO:3226 is the determined cDNA sequence of clone 63298606
SEQ ID NO:3227 is the determined cDNA sequence of clone 63298607
15 SEQ ID NO:3228 is the determined cDNA sequence of clone 63298608
SEQ ID NO:3229 is the determined cDNA sequence of clone 63231735
SEQ ID NO:3230 is the determined cDNA sequence of clone 63231736
SEQ ID NO:3231 is the determined cDNA sequence of clone 63231737
SEQ ID NO:3232 is the determined cDNA sequence of clone 63231738
20 SEQ ID NO:3233 is the determined cDNA sequence of clone 63231739
SEQ ID NO:3234 is the determined cDNA sequence of clone 63231740
SEQ ID NO:3235 is the determined cDNA sequence of clone 63231741
SEQ ID NO:3236 is the determined cDNA sequence of clone 63231742
SEQ ID NO:3237 is the determined cDNA sequence of clone 63231743
25 SEQ ID NO:3238 is the determined cDNA sequence of clone 63231746
SEQ ID NO:3239 is the determined cDNA sequence of clone 63231755
SEQ ID NO:3240 is the determined cDNA sequence of clone 63231756
SEQ ID NO:3241 is the determined cDNA sequence of clone 63231757
SEQ ID NO:3242 is the determined cDNA sequence of clone 63231758
30 SEQ ID NO:3243 is the determined cDNA sequence of clone 63231759
SEQ ID NO:3244 is the determined cDNA sequence of clone 63231760

SEQ ID NO:3245 is the determined cDNA sequence of clone 63231761
SEQ ID NO:3246 is the determined cDNA sequence of clone 63231762
SEQ ID NO:3247 is the determined cDNA sequence of clone 63231763
SEQ ID NO:3248 is the determined cDNA sequence of clone 63231764
5 SEQ ID NO:3249 is the determined cDNA sequence of clone 63231765
SEQ ID NO:3250 is the determined cDNA sequence of clone 63231766
SEQ ID NO:3251 is the determined cDNA sequence of clone 63231767
SEQ ID NO:3252 is the determined cDNA sequence of clone 63231768
SEQ ID NO:3253 is the determined cDNA sequence of clone 63231769
10 SEQ ID NO:3254 is the determined cDNA sequence of clone 63231770
SEQ ID NO:3255 is the determined cDNA sequence of clone 63231771
SEQ ID NO:3256 is the determined cDNA sequence of clone 63231772
SEQ ID NO:3257 is the determined cDNA sequence of clone 63231773
SEQ ID NO:3258 is the determined cDNA sequence of clone 63231774
15 SEQ ID NO:3259 is the determined cDNA sequence of clone 63231775
SEQ ID NO:3260 is the determined cDNA sequence of clone 63231776
SEQ ID NO:3261 is the determined cDNA sequence of clone 63231778
SEQ ID NO:3262 is the determined cDNA sequence of clone 63231779
SEQ ID NO:3263 is the determined cDNA sequence of clone 63231780
20 SEQ ID NO:3264 is the determined cDNA sequence of clone 63231781
SEQ ID NO:3265 is the determined cDNA sequence of clone 63231783
SEQ ID NO:3266 is the determined cDNA sequence of clone 63231784
SEQ ID NO:3267 is the determined cDNA sequence of clone 63231785
SEQ ID NO:3268 is the determined cDNA sequence of clone 63231786
25 SEQ ID NO:3269 is the determined cDNA sequence of clone 63231787
SEQ ID NO:3270 is the determined cDNA sequence of clone 63231788
SEQ ID NO:3271 is the determined cDNA sequence of clone 63231789
SEQ ID NO:3272 is the determined cDNA sequence of clone 63231790
SEQ ID NO:3273 is the determined cDNA sequence of clone 63231791
30 SEQ ID NO:3274 is the determined cDNA sequence of clone 63231792
SEQ ID NO:3275 is the determined cDNA sequence of clone 63231793

SEQ ID NO:3276 is the determined cDNA sequence of clone 63231794
SEQ ID NO:3277 is the determined cDNA sequence of clone 63231795
SEQ ID NO:3278 is the determined cDNA sequence of clone 63231796
SEQ ID NO:3279 is the determined cDNA sequence of clone 63231797
5 SEQ ID NO:3280 is the determined cDNA sequence of clone 63231798
SEQ ID NO:3281 is the determined cDNA sequence of clone 63231799
SEQ ID NO:3282 is the determined cDNA sequence of clone 63231800
SEQ ID NO:3283 is the determined cDNA sequence of clone 63231801
SEQ ID NO:3284 is the determined cDNA sequence of clone 63231802
10 SEQ ID NO:3285 is the determined cDNA sequence of clone 63231803
SEQ ID NO:3286 is the determined cDNA sequence of clone 63231804
SEQ ID NO:3287 is the determined cDNA sequence of clone 63231805
SEQ ID NO:3288 is the determined cDNA sequence of clone 63231806
SEQ ID NO:3289 is the determined cDNA sequence of clone 63231809
15 SEQ ID NO:3290 is the determined cDNA sequence of clone 63231810
SEQ ID NO:3291 is the determined cDNA sequence of clone 63231811
SEQ ID NO:3292 is the determined cDNA sequence of clone 63231812
SEQ ID NO:3293 is the determined cDNA sequence of clone 63231813
SEQ ID NO:3294 is the determined cDNA sequence of clone 63231814
20 SEQ ID NO:3295 is the determined cDNA sequence of clone 63231815
SEQ ID NO:3296 is the determined cDNA sequence of clone 63231816
SEQ ID NO:3297 is the determined cDNA sequence of clone 63231817
SEQ ID NO:3298 is the determined cDNA sequence of clone 63231818
SEQ ID NO:3299 is the determined cDNA sequence of clone 63231819
25 SEQ ID NO:3300 is the determined cDNA sequence of clone 63231821
SEQ ID NO:3301 is the determined cDNA sequence of clone 63231822
SEQ ID NO:3302 is the determined cDNA sequence of clone 63231823
SEQ ID NO:3303 is the determined cDNA sequence of clone 63231824
SEQ ID NO:3304 is the determined cDNA sequence of clone 63231825
30 SEQ ID NO:3305 is the determined cDNA sequence of clone 63250511
SEQ ID NO:3306 is the determined cDNA sequence of clone 63250512

SEQ ID NO:3307 is the determined cDNA sequence of clone 63250513
SEQ ID NO:3308 is the determined cDNA sequence of clone 63250514
SEQ ID NO:3309 is the determined cDNA sequence of clone 63250516
SEQ ID NO:3310 is the determined cDNA sequence of clone 63250517
5 SEQ ID NO:3311 is the determined cDNA sequence of clone 63250518
SEQ ID NO:3312 is the determined cDNA sequence of clone 63250519
SEQ ID NO:3313 is the determined cDNA sequence of clone 63250520
SEQ ID NO:3314 is the determined cDNA sequence of clone 63250521
SEQ ID NO:3315 is the determined cDNA sequence of clone 63250525
10 SEQ ID NO:3316 is the determined cDNA sequence of clone 63250526
SEQ ID NO:3317 is the determined cDNA sequence of clone 63250527
SEQ ID NO:3318 is the determined cDNA sequence of clone 63250528
SEQ ID NO:3319 is the determined cDNA sequence of clone 63250529
SEQ ID NO:3320 is the determined cDNA sequence of clone 63250530
15 SEQ ID NO:3321 is the determined cDNA sequence of clone 63250531
SEQ ID NO:3322 is the determined cDNA sequence of clone 63250532
SEQ ID NO:3323 is the determined cDNA sequence of clone 63250533
SEQ ID NO:3324 is the determined cDNA sequence of clone 63250535
SEQ ID NO:3325 is the determined cDNA sequence of clone 63250536
20 SEQ ID NO:3326 is the determined cDNA sequence of clone 63250537
SEQ ID NO:3327 is the determined cDNA sequence of clone 63250538
SEQ ID NO:3328 is the determined cDNA sequence of clone 63250540
SEQ ID NO:3329 is the determined cDNA sequence of clone 63250541
SEQ ID NO:3330 is the determined cDNA sequence of clone 63250542
25 SEQ ID NO:3331 is the determined cDNA sequence of clone 63250543
SEQ ID NO:3332 is the determined cDNA sequence of clone 63250544
SEQ ID NO:3333 is the determined cDNA sequence of clone 63250545
SEQ ID NO:3334 is the determined cDNA sequence of clone 63250546
SEQ ID NO:3335 is the determined cDNA sequence of clone 63250547
30 SEQ ID NO:3336 is the determined cDNA sequence of clone 63250548
SEQ ID NO:3337 is the determined cDNA sequence of clone 63250549

SEQ ID NO:3338 is the determined cDNA sequence of clone 63250550
SEQ ID NO:3339 is the determined cDNA sequence of clone 63250551
SEQ ID NO:3340 is the determined cDNA sequence of clone 63250552
SEQ ID NO:3341 is the determined cDNA sequence of clone 63250553
5 SEQ ID NO:3342 is the determined cDNA sequence of clone 63250554
SEQ ID NO:3343 is the determined cDNA sequence of clone 63250555
SEQ ID NO:3344 is the determined cDNA sequence of clone 63250556
SEQ ID NO:3345 is the determined cDNA sequence of clone 63250558
SEQ ID NO:3346 is the determined cDNA sequence of clone 63250559
10 SEQ ID NO:3347 is the determined cDNA sequence of clone 63250560
SEQ ID NO:3348 is the determined cDNA sequence of clone 63250561
SEQ ID NO:3349 is the determined cDNA sequence of clone 63250562
SEQ ID NO:3350 is the determined cDNA sequence of clone 63250563
SEQ ID NO:3351 is the determined cDNA sequence of clone 63250564
15 SEQ ID NO:3352 is the determined cDNA sequence of clone 63250566
SEQ ID NO:3353 is the determined cDNA sequence of clone 63250567
SEQ ID NO:3354 is the determined cDNA sequence of clone 63250568
SEQ ID NO:3355 is the determined cDNA sequence of clone 63250569
SEQ ID NO:3356 is the determined cDNA sequence of clone 63250570
20 SEQ ID NO:3357 is the determined cDNA sequence of clone 63250572
SEQ ID NO:3358 is the determined cDNA sequence of clone 63250573
SEQ ID NO:3359 is the determined cDNA sequence of clone 63250574
SEQ ID NO:3360 is the determined cDNA sequence of clone 63250575
SEQ ID NO:3361 is the determined cDNA sequence of clone 63250576
25 SEQ ID NO:3362 is the determined cDNA sequence of clone 63250577
SEQ ID NO:3363 is the determined cDNA sequence of clone 63250578
SEQ ID NO:3364 is the determined cDNA sequence of clone 63250579
SEQ ID NO:3365 is the determined cDNA sequence of clone 63250580
SEQ ID NO:3366 is the determined cDNA sequence of clone 63250581
30 SEQ ID NO:3367 is the determined cDNA sequence of clone 63250582
SEQ ID NO:3368 is the determined cDNA sequence of clone 63250583

SEQ ID NO:3369 is the determined cDNA sequence of clone 63250584
SEQ ID NO:3370 is the determined cDNA sequence of clone 63250585
SEQ ID NO:3371 is the determined cDNA sequence of clone 63250586
SEQ ID NO:3372 is the determined cDNA sequence of clone 63250587
5 SEQ ID NO:3373 is the determined cDNA sequence of clone 63250588
SEQ ID NO:3374 is the determined cDNA sequence of clone 63250589
SEQ ID NO:3375 is the determined cDNA sequence of clone 63250590
SEQ ID NO:3376 is the determined cDNA sequence of clone 63250591
SEQ ID NO:3377 is the determined cDNA sequence of clone 63250592
10 SEQ ID NO:3378 is the determined cDNA sequence of clone 63250593
SEQ ID NO:3379 is the determined cDNA sequence of clone 63250594
SEQ ID NO:3380 is the determined cDNA sequence of clone 63250595
SEQ ID NO:3381 is the determined cDNA sequence of clone 63250596
SEQ ID NO:3382 is the determined cDNA sequence of clone 63250597
15 SEQ ID NO:3383 is the determined cDNA sequence of clone 63250598
SEQ ID NO:3384 is the determined cDNA sequence of clone 63250599
SEQ ID NO:3385 is the determined cDNA sequence of clone 63250600
SEQ ID NO:3386 is the determined cDNA sequence of clone 63250601
SEQ ID NO:3387 is the determined cDNA sequence of clone 63250602
20 SEQ ID NO:3388 is the determined cDNA sequence of clone 63250603
SEQ ID NO:3389 is the determined cDNA sequence of clone 63231826
SEQ ID NO:3390 is the determined cDNA sequence of clone 63231827
SEQ ID NO:3391 is the determined cDNA sequence of clone 63231828
SEQ ID NO:3392 is the determined cDNA sequence of clone 63231829
25 SEQ ID NO:3393 is the determined cDNA sequence of clone 63231830
SEQ ID NO:3394 is the determined cDNA sequence of clone 63231831
SEQ ID NO:3395 is the determined cDNA sequence of clone 63231832
SEQ ID NO:3396 is the determined cDNA sequence of clone 63231833
SEQ ID NO:3397 is the determined cDNA sequence of clone 63231834
30 SEQ ID NO:3398 is the determined cDNA sequence of clone 63231835
SEQ ID NO:3399 is the determined cDNA sequence of clone 63231836

SEQ ID NO:3400 is the determined cDNA sequence of clone 63231837
SEQ ID NO:3401 is the determined cDNA sequence of clone 63231838
SEQ ID NO:3402 is the determined cDNA sequence of clone 63231839
SEQ ID NO:3403 is the determined cDNA sequence of clone 63231840
5 SEQ ID NO:3404 is the determined cDNA sequence of clone 63231841
SEQ ID NO:3405 is the determined cDNA sequence of clone 63231842
SEQ ID NO:3406 is the determined cDNA sequence of clone 63231843
SEQ ID NO:3407 is the determined cDNA sequence of clone 63231844
SEQ ID NO:3408 is the determined cDNA sequence of clone 63231845
10 SEQ ID NO:3409 is the determined cDNA sequence of clone 63231846
SEQ ID NO:3410 is the determined cDNA sequence of clone 63231847
SEQ ID NO:3411 is the determined cDNA sequence of clone 63231848
SEQ ID NO:3412 is the determined cDNA sequence of clone 63231849
SEQ ID NO:3413 is the determined cDNA sequence of clone 63231850
15 SEQ ID NO:3414 is the determined cDNA sequence of clone 63231851
SEQ ID NO:3415 is the determined cDNA sequence of clone 63231852
SEQ ID NO:3416 is the determined cDNA sequence of clone 63231853
SEQ ID NO:3417 is the determined cDNA sequence of clone 63231854
SEQ ID NO:3418 is the determined cDNA sequence of clone 63231855
20 SEQ ID NO:3419 is the determined cDNA sequence of clone 63231856
SEQ ID NO:3420 is the determined cDNA sequence of clone 63231857
SEQ ID NO:3421 is the determined cDNA sequence of clone 63231858
SEQ ID NO:3422 is the determined cDNA sequence of clone 63231859
SEQ ID NO:3423 is the determined cDNA sequence of clone 63231860
25 SEQ ID NO:3424 is the determined cDNA sequence of clone 63231861
SEQ ID NO:3425 is the determined cDNA sequence of clone 63231862
SEQ ID NO:3426 is the determined cDNA sequence of clone 63231863
SEQ ID NO:3427 is the determined cDNA sequence of clone 63231864
SEQ ID NO:3428 is the determined cDNA sequence of clone 63231865
30 SEQ ID NO:3429 is the determined cDNA sequence of clone 63231866
SEQ ID NO:3430 is the determined cDNA sequence of clone 63231867

SEQ ID NO:3431 is the determined cDNA sequence of clone 63231868
SEQ ID NO:3432 is the determined cDNA sequence of clone 63231869
SEQ ID NO:3433 is the determined cDNA sequence of clone 63231871
SEQ ID NO:3434 is the determined cDNA sequence of clone 63231872
5 SEQ ID NO:3435 is the determined cDNA sequence of clone 63231873
SEQ ID NO:3436 is the determined cDNA sequence of clone 63231875
SEQ ID NO:3437 is the determined cDNA sequence of clone 63231876
SEQ ID NO:3438 is the determined cDNA sequence of clone 63231877
SEQ ID NO:3439 is the determined cDNA sequence of clone 63231878
10 SEQ ID NO:3440 is the determined cDNA sequence of clone 63231879
SEQ ID NO:3441 is the determined cDNA sequence of clone 63231880
SEQ ID NO:3442 is the determined cDNA sequence of clone 63231881
SEQ ID NO:3443 is the determined cDNA sequence of clone 63231882
SEQ ID NO:3444 is the determined cDNA sequence of clone 63231883
15 SEQ ID NO:3445 is the determined cDNA sequence of clone 63231884
SEQ ID NO:3446 is the determined cDNA sequence of clone 63231885
SEQ ID NO:3447 is the determined cDNA sequence of clone 63231886
SEQ ID NO:3448 is the determined cDNA sequence of clone 63231887
SEQ ID NO:3449 is the determined cDNA sequence of clone 63231888
20 SEQ ID NO:3450 is the determined cDNA sequence of clone 63231889
SEQ ID NO:3451 is the determined cDNA sequence of clone 63231890
SEQ ID NO:3452 is the determined cDNA sequence of clone 63231891
SEQ ID NO:3453 is the determined cDNA sequence of clone 63231892
SEQ ID NO:3454 is the determined cDNA sequence of clone 63231893
25 SEQ ID NO:3455 is the determined cDNA sequence of clone 63231894
SEQ ID NO:3456 is the determined cDNA sequence of clone 63231895
SEQ ID NO:3457 is the determined cDNA sequence of clone 63231898
SEQ ID NO:3458 is the determined cDNA sequence of clone 63231899
SEQ ID NO:3459 is the determined cDNA sequence of clone 63231900
30 SEQ ID NO:3460 is the determined cDNA sequence of clone 63231901
SEQ ID NO:3461 is the determined cDNA sequence of clone 63231902

SEQ ID NO:3462 is the determined cDNA sequence of clone 63231903
SEQ ID NO:3463 is the determined cDNA sequence of clone 63231904
SEQ ID NO:3464 is the determined cDNA sequence of clone 63231905
SEQ ID NO:3465 is the determined cDNA sequence of clone 63231906
5 SEQ ID NO:3466 is the determined cDNA sequence of clone 63231907
SEQ ID NO:3467 is the determined cDNA sequence of clone 63231908
SEQ ID NO:3468 is the determined cDNA sequence of clone 63231910
SEQ ID NO:3469 is the determined cDNA sequence of clone 63231911
SEQ ID NO:3470 is the determined cDNA sequence of clone 63231913
10 SEQ ID NO:3471 is the determined cDNA sequence of clone 63231914
SEQ ID NO:3472 is the determined cDNA sequence of clone 63231915
SEQ ID NO:3473 is the determined cDNA sequence of clone 63231917
SEQ ID NO:3474 is the determined cDNA sequence of clone 63231918
SEQ ID NO:3475 is the determined cDNA sequence of clone 63231548
15 SEQ ID NO:3476 is the determined cDNA sequence of clone 63231549
SEQ ID NO:3477 is the determined cDNA sequence of clone 63231550
SEQ ID NO:3478 is the determined cDNA sequence of clone 63231551
SEQ ID NO:3479 is the determined cDNA sequence of clone 63231552
SEQ ID NO:3480 is the determined cDNA sequence of clone 63231553
20 SEQ ID NO:3481 is the determined cDNA sequence of clone 63231554
SEQ ID NO:3482 is the determined cDNA sequence of clone 63231555
SEQ ID NO:3483 is the determined cDNA sequence of clone 63231557
SEQ ID NO:3484 is the determined cDNA sequence of clone 63231558
SEQ ID NO:3485 is the determined cDNA sequence of clone 63231559
25 SEQ ID NO:3486 is the determined cDNA sequence of clone 63231560
SEQ ID NO:3487 is the determined cDNA sequence of clone 63231561
SEQ ID NO:3488 is the determined cDNA sequence of clone 63231562
SEQ ID NO:3489 is the determined cDNA sequence of clone 63231563
SEQ ID NO:3490 is the determined cDNA sequence of clone 63231564
30 SEQ ID NO:3491 is the determined cDNA sequence of clone 63231565
SEQ ID NO:3492 is the determined cDNA sequence of clone 63231566

SEQ ID NO:3493 is the determined cDNA sequence of clone 63231567
SEQ ID NO:3494 is the determined cDNA sequence of clone 63231568
SEQ ID NO:3495 is the determined cDNA sequence of clone 63231569
SEQ ID NO:3496 is the determined cDNA sequence of clone 63231571
5 SEQ ID NO:3497 is the determined cDNA sequence of clone 63231572
SEQ ID NO:3498 is the determined cDNA sequence of clone 63231573
SEQ ID NO:3499 is the determined cDNA sequence of clone 63231574
SEQ ID NO:3500 is the determined cDNA sequence of clone 63231575
SEQ ID NO:3501 is the determined cDNA sequence of clone 63231576
10 SEQ ID NO:3502 is the determined cDNA sequence of clone 63231577
SEQ ID NO:3503 is the determined cDNA sequence of clone 63231578
SEQ ID NO:3504 is the determined cDNA sequence of clone 63231579
SEQ ID NO:3505 is the determined cDNA sequence of clone 63231580
SEQ ID NO:3506 is the determined cDNA sequence of clone 63231581
15 SEQ ID NO:3507 is the determined cDNA sequence of clone 63231582
SEQ ID NO:3508 is the determined cDNA sequence of clone 63231583
SEQ ID NO:3509 is the determined cDNA sequence of clone 63231584
SEQ ID NO:3510 is the determined cDNA sequence of clone 63231585
SEQ ID NO:3511 is the determined cDNA sequence of clone 63231586
20 SEQ ID NO:3512 is the determined cDNA sequence of clone 63231587
SEQ ID NO:3513 is the determined cDNA sequence of clone 63231588
SEQ ID NO:3514 is the determined cDNA sequence of clone 63231589
SEQ ID NO:3515 is the determined cDNA sequence of clone 63231590
SEQ ID NO:3516 is the determined cDNA sequence of clone 63231591
25 SEQ ID NO:3517 is the determined cDNA sequence of clone 63231592
SEQ ID NO:3518 is the determined cDNA sequence of clone 63231593
SEQ ID NO:3519 is the determined cDNA sequence of clone 63231594
SEQ ID NO:3520 is the determined cDNA sequence of clone 63231595
SEQ ID NO:3521 is the determined cDNA sequence of clone 63231596
30 SEQ ID NO:3522 is the determined cDNA sequence of clone 63231597
SEQ ID NO:3523 is the determined cDNA sequence of clone 63231598

SEQ ID NO:3524 is the determined cDNA sequence of clone 63231599
SEQ ID NO:3525 is the determined cDNA sequence of clone 63231600
SEQ ID NO:3526 is the determined cDNA sequence of clone 63231601
SEQ ID NO:3527 is the determined cDNA sequence of clone 63231602
5 SEQ ID NO:3528 is the determined cDNA sequence of clone 63231603
SEQ ID NO:3529 is the determined cDNA sequence of clone 63231604
SEQ ID NO:3530 is the determined cDNA sequence of clone 63231605
SEQ ID NO:3531 is the determined cDNA sequence of clone 63231606
SEQ ID NO:3532 is the determined cDNA sequence of clone 63231607
10 SEQ ID NO:3533 is the determined cDNA sequence of clone 63231608
SEQ ID NO:3534 is the determined cDNA sequence of clone 63231609
SEQ ID NO:3535 is the determined cDNA sequence of clone 63231610
SEQ ID NO:3536 is the determined cDNA sequence of clone 63231611
SEQ ID NO:3537 is the determined cDNA sequence of clone 63231612
15 SEQ ID NO:3538 is the determined cDNA sequence of clone 63231613
SEQ ID NO:3539 is the determined cDNA sequence of clone 63231614
SEQ ID NO:3540 is the determined cDNA sequence of clone 63231615
SEQ ID NO:3541 is the determined cDNA sequence of clone 63231616
SEQ ID NO:3542 is the determined cDNA sequence of clone 63231617
20 SEQ ID NO:3543 is the determined cDNA sequence of clone 63231618
SEQ ID NO:3544 is the determined cDNA sequence of clone 63231619
SEQ ID NO:3545 is the determined cDNA sequence of clone 63231620
SEQ ID NO:3546 is the determined cDNA sequence of clone 63231621
SEQ ID NO:3547 is the determined cDNA sequence of clone 63231623
25 SEQ ID NO:3548 is the determined cDNA sequence of clone 63231625
SEQ ID NO:3549 is the determined cDNA sequence of clone 63231626
SEQ ID NO:3550 is the determined cDNA sequence of clone 63231627
SEQ ID NO:3551 is the determined cDNA sequence of clone 63231628
SEQ ID NO:3552 is the determined cDNA sequence of clone 63231629
30 SEQ ID NO:3553 is the determined cDNA sequence of clone 63231630
SEQ ID NO:3554 is the determined cDNA sequence of clone 63231631

SEQ ID NO:3555 is the determined cDNA sequence of clone 63231632
SEQ ID NO:3556 is the determined cDNA sequence of clone 63231633
SEQ ID NO:3557 is the determined cDNA sequence of clone 63231634
SEQ ID NO:3558 is the determined cDNA sequence of clone 63231635
5 SEQ ID NO:3559 is the determined cDNA sequence of clone 63231636
SEQ ID NO:3560 is the determined cDNA sequence of clone 63231637
SEQ ID NO:3561 is the determined cDNA sequence of clone 63231638
SEQ ID NO:3562 is the determined cDNA sequence of clone 63231639
SEQ ID NO:3563 is the determined cDNA sequence of clone 63298237
10 SEQ ID NO:3564 is the determined cDNA sequence of clone 63298238
SEQ ID NO:3565 is the determined cDNA sequence of clone 63298239
SEQ ID NO:3566 is the determined cDNA sequence of clone 63298240
SEQ ID NO:3567 is the determined cDNA sequence of clone 63298241
SEQ ID NO:3568 is the determined cDNA sequence of clone 63298242
15 SEQ ID NO:3569 is the determined cDNA sequence of clone 63298243
SEQ ID NO:3570 is the determined cDNA sequence of clone 63298244
SEQ ID NO:3571 is the determined cDNA sequence of clone 63298245
SEQ ID NO:3572 is the determined cDNA sequence of clone 63298246
SEQ ID NO:3573 is the determined cDNA sequence of clone 63298247
20 SEQ ID NO:3574 is the determined cDNA sequence of clone 63298248
SEQ ID NO:3575 is the determined cDNA sequence of clone 63298249
SEQ ID NO:3576 is the determined cDNA sequence of clone 63298250
SEQ ID NO:3577 is the determined cDNA sequence of clone 63298251
SEQ ID NO:3578 is the determined cDNA sequence of clone 63298252
25 SEQ ID NO:3579 is the determined cDNA sequence of clone 63298253
SEQ ID NO:3580 is the determined cDNA sequence of clone 63298254
SEQ ID NO:3581 is the determined cDNA sequence of clone 63298255
SEQ ID NO:3582 is the determined cDNA sequence of clone 63298256
SEQ ID NO:3583 is the determined cDNA sequence of clone 63298257
30 SEQ ID NO:3584 is the determined cDNA sequence of clone 63298258
SEQ ID NO:3585 is the determined cDNA sequence of clone 63298259

SEQ ID NO:3586 is the determined cDNA sequence of clone 63298261
SEQ ID NO:3587 is the determined cDNA sequence of clone 63298262
SEQ ID NO:3588 is the determined cDNA sequence of clone 63298263
SEQ ID NO:3589 is the determined cDNA sequence of clone 63298264
5 SEQ ID NO:3590 is the determined cDNA sequence of clone 63298265
SEQ ID NO:3591 is the determined cDNA sequence of clone 63298266
SEQ ID NO:3592 is the determined cDNA sequence of clone 63298267
SEQ ID NO:3593 is the determined cDNA sequence of clone 63298268
SEQ ID NO:3594 is the determined cDNA sequence of clone 63298269
10 SEQ ID NO:3595 is the determined cDNA sequence of clone 63298270
SEQ ID NO:3596 is the determined cDNA sequence of clone 63298271
SEQ ID NO:3597 is the determined cDNA sequence of clone 63298273
SEQ ID NO:3598 is the determined cDNA sequence of clone 63298274
SEQ ID NO:3599 is the determined cDNA sequence of clone 63298275
15 SEQ ID NO:3600 is the determined cDNA sequence of clone 63298276
SEQ ID NO:3601 is the determined cDNA sequence of clone 63298278
SEQ ID NO:3602 is the determined cDNA sequence of clone 63298279
SEQ ID NO:3603 is the determined cDNA sequence of clone 63298280
SEQ ID NO:3604 is the determined cDNA sequence of clone 63298281
20 SEQ ID NO:3605 is the determined cDNA sequence of clone 63298282
SEQ ID NO:3606 is the determined cDNA sequence of clone 63298284
SEQ ID NO:3607 is the determined cDNA sequence of clone 63298287
SEQ ID NO:3608 is the determined cDNA sequence of clone 63298288
SEQ ID NO:3609 is the determined cDNA sequence of clone 63298289
25 SEQ ID NO:3610 is the determined cDNA sequence of clone 63298290
SEQ ID NO:3611 is the determined cDNA sequence of clone 63298291
SEQ ID NO:3612 is the determined cDNA sequence of clone 63298292
SEQ ID NO:3613 is the determined cDNA sequence of clone 63298293
SEQ ID NO:3614 is the determined cDNA sequence of clone 63298294
30 SEQ ID NO:3615 is the determined cDNA sequence of clone 63298295
SEQ ID NO:3616 is the determined cDNA sequence of clone 63298296

SEQ ID NO:3617 is the determined cDNA sequence of clone 63298297
SEQ ID NO:3618 is the determined cDNA sequence of clone 63298299
SEQ ID NO:3619 is the determined cDNA sequence of clone 63298300
SEQ ID NO:3620 is the determined cDNA sequence of clone 63298301
5 SEQ ID NO:3621 is the determined cDNA sequence of clone 63298303
SEQ ID NO:3622 is the determined cDNA sequence of clone 63298304
SEQ ID NO:3623 is the determined cDNA sequence of clone 63298307
SEQ ID NO:3624 is the determined cDNA sequence of clone 63298308
SEQ ID NO:3625 is the determined cDNA sequence of clone 63298309
10 SEQ ID NO:3626 is the determined cDNA sequence of clone 63298310
SEQ ID NO:3627 is the determined cDNA sequence of clone 63298311
SEQ ID NO:3628 is the determined cDNA sequence of clone 63298313
SEQ ID NO:3629 is the determined cDNA sequence of clone 63298314
SEQ ID NO:3630 is the determined cDNA sequence of clone 63298315
15 SEQ ID NO:3631 is the determined cDNA sequence of clone 63298316
SEQ ID NO:3632 is the determined cDNA sequence of clone 63298317
SEQ ID NO:3633 is the determined cDNA sequence of clone 63298318
SEQ ID NO:3634 is the determined cDNA sequence of clone 63298319
SEQ ID NO:3635 is the determined cDNA sequence of clone 63298321
20 SEQ ID NO:3636 is the determined cDNA sequence of clone 63298323
SEQ ID NO:3637 is the determined cDNA sequence of clone 63298324
SEQ ID NO:3638 is the determined cDNA sequence of clone 63298325
SEQ ID NO:3639 is the determined cDNA sequence of clone 63298326
SEQ ID NO:3640 is the determined cDNA sequence of clone 63298327
25 SEQ ID NO:3641 is the determined cDNA sequence of clone 63298328
SEQ ID NO:3642 is the determined cDNA sequence of clone 63298329
SEQ ID NO:3643 is the determined cDNA sequence of clone 63298424
SEQ ID NO:3644 is the determined cDNA sequence of clone 63298425
SEQ ID NO:3645 is the determined cDNA sequence of clone 63298426
30 SEQ ID NO:3646 is the determined cDNA sequence of clone 63298427
SEQ ID NO:3647 is the determined cDNA sequence of clone 63298428

SEQ ID NO:3648 is the determined cDNA sequence of clone 63298429
SEQ ID NO:3649 is the determined cDNA sequence of clone 63298430
SEQ ID NO:3650 is the determined cDNA sequence of clone 63298431
SEQ ID NO:3651 is the determined cDNA sequence of clone 63298432
5 SEQ ID NO:3652 is the determined cDNA sequence of clone 63298433
SEQ ID NO:3653 is the determined cDNA sequence of clone 63298434
SEQ ID NO:3654 is the determined cDNA sequence of clone 63298435
SEQ ID NO:3655 is the determined cDNA sequence of clone 63298436
SEQ ID NO:3656 is the determined cDNA sequence of clone 63298437
10 SEQ ID NO:3657 is the determined cDNA sequence of clone 63298438
SEQ ID NO:3658 is the determined cDNA sequence of clone 63298439
SEQ ID NO:3659 is the determined cDNA sequence of clone 63298440
SEQ ID NO:3660 is the determined cDNA sequence of clone 63298441
SEQ ID NO:3661 is the determined cDNA sequence of clone 63298443
15 SEQ ID NO:3662 is the determined cDNA sequence of clone 63298444
SEQ ID NO:3663 is the determined cDNA sequence of clone 63298445
SEQ ID NO:3664 is the determined cDNA sequence of clone 63298446
SEQ ID NO:3665 is the determined cDNA sequence of clone 63298447
SEQ ID NO:3666 is the determined cDNA sequence of clone 63298448
20 SEQ ID NO:3667 is the determined cDNA sequence of clone 63298449
SEQ ID NO:3668 is the determined cDNA sequence of clone 63298451
SEQ ID NO:3669 is the determined cDNA sequence of clone 63298452
SEQ ID NO:3670 is the determined cDNA sequence of clone 63298453
SEQ ID NO:3671 is the determined cDNA sequence of clone 63298454
25 SEQ ID NO:3672 is the determined cDNA sequence of clone 63298455
SEQ ID NO:3673 is the determined cDNA sequence of clone 63298456
SEQ ID NO:3674 is the determined cDNA sequence of clone 63298457
SEQ ID NO:3675 is the determined cDNA sequence of clone 63298458
SEQ ID NO:3676 is the determined cDNA sequence of clone 63298459
30 SEQ ID NO:3677 is the determined cDNA sequence of clone 63298460
SEQ ID NO:3678 is the determined cDNA sequence of clone 63298461

SEQ ID NO:3679 is the determined cDNA sequence of clone 63298462
SEQ ID NO:3680 is the determined cDNA sequence of clone 63298463
SEQ ID NO:3681 is the determined cDNA sequence of clone 63298464
SEQ ID NO:3682 is the determined cDNA sequence of clone 63298465
5 SEQ ID NO:3683 is the determined cDNA sequence of clone 63298466
SEQ ID NO:3684 is the determined cDNA sequence of clone 63298468
SEQ ID NO:3685 is the determined cDNA sequence of clone 63298469
SEQ ID NO:3686 is the determined cDNA sequence of clone 63298470
SEQ ID NO:3687 is the determined cDNA sequence of clone 63298471
10 SEQ ID NO:3688 is the determined cDNA sequence of clone 63298472
SEQ ID NO:3689 is the determined cDNA sequence of clone 63298473
SEQ ID NO:3690 is the determined cDNA sequence of clone 63298474
SEQ ID NO:3691 is the determined cDNA sequence of clone 63298475
SEQ ID NO:3692 is the determined cDNA sequence of clone 63298476
15 SEQ ID NO:3693 is the determined cDNA sequence of clone 63298477
SEQ ID NO:3694 is the determined cDNA sequence of clone 63298478
SEQ ID NO:3695 is the determined cDNA sequence of clone 63298481
SEQ ID NO:3696 is the determined cDNA sequence of clone 63298482
SEQ ID NO:3697 is the determined cDNA sequence of clone 63298483
20 SEQ ID NO:3698 is the determined cDNA sequence of clone 63298484
SEQ ID NO:3699 is the determined cDNA sequence of clone 63298485
SEQ ID NO:3700 is the determined cDNA sequence of clone 63298486
SEQ ID NO:3701 is the determined cDNA sequence of clone 63298487
SEQ ID NO:3702 is the determined cDNA sequence of clone 63298488
25 SEQ ID NO:3703 is the determined cDNA sequence of clone 63298489
SEQ ID NO:3704 is the determined cDNA sequence of clone 63298490
SEQ ID NO:3705 is the determined cDNA sequence of clone 63298491
SEQ ID NO:3706 is the determined cDNA sequence of clone 63298492
SEQ ID NO:3707 is the determined cDNA sequence of clone 63298493
30 SEQ ID NO:3708 is the determined cDNA sequence of clone 63298494
SEQ ID NO:3709 is the determined cDNA sequence of clone 63298495

SEQ ID NO:3710 is the determined cDNA sequence of clone 63298496
SEQ ID NO:3711 is the determined cDNA sequence of clone 63298497
SEQ ID NO:3712 is the determined cDNA sequence of clone 63298498
SEQ ID NO:3713 is the determined cDNA sequence of clone 63298499
5 SEQ ID NO:3714 is the determined cDNA sequence of clone 63298500
SEQ ID NO:3715 is the determined cDNA sequence of clone 63298501
SEQ ID NO:3716 is the determined cDNA sequence of clone 63298502
SEQ ID NO:3717 is the determined cDNA sequence of clone 63298504
SEQ ID NO:3718 is the determined cDNA sequence of clone 63298505
10 SEQ ID NO:3719 is the determined cDNA sequence of clone 63298506
SEQ ID NO:3720 is the determined cDNA sequence of clone 63298507
SEQ ID NO:3721 is the determined cDNA sequence of clone 63298508
SEQ ID NO:3722 is the determined cDNA sequence of clone 63298509
SEQ ID NO:3723 is the determined cDNA sequence of clone 63298510
15 SEQ ID NO:3724 is the determined cDNA sequence of clone 63298511
SEQ ID NO:3725 is the determined cDNA sequence of clone 63298512
SEQ ID NO:3726 is the determined cDNA sequence of clone 63298513
SEQ ID NO:3727 is the determined cDNA sequence of clone 63298514
SEQ ID NO:3728 is the determined cDNA sequence of clone 63298515
20 SEQ ID NO:3729 is the determined cDNA sequence of clone 63299075
SEQ ID NO:3730 is the determined cDNA sequence of clone 63299076
SEQ ID NO:3731 is the determined cDNA sequence of clone 63299077
SEQ ID NO:3732 is the determined cDNA sequence of clone 63299078
SEQ ID NO:3733 is the determined cDNA sequence of clone 63299079
25 SEQ ID NO:3734 is the determined cDNA sequence of clone 63299080
SEQ ID NO:3735 is the determined cDNA sequence of clone 63299081
SEQ ID NO:3736 is the determined cDNA sequence of clone 63299082
SEQ ID NO:3737 is the determined cDNA sequence of clone 63299083
SEQ ID NO:3738 is the determined cDNA sequence of clone 63299084
30 SEQ ID NO:3739 is the determined cDNA sequence of clone 63299085
SEQ ID NO:3740 is the determined cDNA sequence of clone 63299086

SEQ ID NO:3741 is the determined cDNA sequence of clone 63299087
SEQ ID NO:3742 is the determined cDNA sequence of clone 63299088
SEQ ID NO:3743 is the determined cDNA sequence of clone 63299089
SEQ ID NO:3744 is the determined cDNA sequence of clone 63299090
5 SEQ ID NO:3745 is the determined cDNA sequence of clone 63299092
SEQ ID NO:3746 is the determined cDNA sequence of clone 63299093
SEQ ID NO:3747 is the determined cDNA sequence of clone 63299094
SEQ ID NO:3748 is the determined cDNA sequence of clone 63299095
SEQ ID NO:3749 is the determined cDNA sequence of clone 63299096
10 SEQ ID NO:3750 is the determined cDNA sequence of clone 63299097
SEQ ID NO:3751 is the determined cDNA sequence of clone 63299099
SEQ ID NO:3752 is the determined cDNA sequence of clone 63299100
SEQ ID NO:3753 is the determined cDNA sequence of clone 63299101
SEQ ID NO:3754 is the determined cDNA sequence of clone 63299102
15 SEQ ID NO:3755 is the determined cDNA sequence of clone 63299104
SEQ ID NO:3756 is the determined cDNA sequence of clone 63299105
SEQ ID NO:3757 is the determined cDNA sequence of clone 63299106
SEQ ID NO:3758 is the determined cDNA sequence of clone 63299107
SEQ ID NO:3759 is the determined cDNA sequence of clone 63299108
20 SEQ ID NO:3760 is the determined cDNA sequence of clone 63299109
SEQ ID NO:3761 is the determined cDNA sequence of clone 63299110
SEQ ID NO:3762 is the determined cDNA sequence of clone 63299111
SEQ ID NO:3763 is the determined cDNA sequence of clone 63299112
SEQ ID NO:3764 is the determined cDNA sequence of clone 63299113
25 SEQ ID NO:3765 is the determined cDNA sequence of clone 63299114
SEQ ID NO:3766 is the determined cDNA sequence of clone 63299116
SEQ ID NO:3767 is the determined cDNA sequence of clone 63299117
SEQ ID NO:3768 is the determined cDNA sequence of clone 63299118
SEQ ID NO:3769 is the determined cDNA sequence of clone 63299120
30 SEQ ID NO:3770 is the determined cDNA sequence of clone 63299122
SEQ ID NO:3771 is the determined cDNA sequence of clone 63299123

SEQ ID NO:3772 is the determined cDNA sequence of clone 63299125
SEQ ID NO:3773 is the determined cDNA sequence of clone 63299126
SEQ ID NO:3774 is the determined cDNA sequence of clone 63299128
SEQ ID NO:3775 is the determined cDNA sequence of clone 63299129
5 SEQ ID NO:3776 is the determined cDNA sequence of clone 63299130
SEQ ID NO:3777 is the determined cDNA sequence of clone 63299131
SEQ ID NO:3778 is the determined cDNA sequence of clone 63299132
SEQ ID NO:3779 is the determined cDNA sequence of clone 63299134
SEQ ID NO:3780 is the determined cDNA sequence of clone 63299135
10 SEQ ID NO:3781 is the determined cDNA sequence of clone 63299136
SEQ ID NO:3782 is the determined cDNA sequence of clone 63299137
SEQ ID NO:3783 is the determined cDNA sequence of clone 63299138
SEQ ID NO:3784 is the determined cDNA sequence of clone 63299139
SEQ ID NO:3785 is the determined cDNA sequence of clone 63299140
15 SEQ ID NO:3786 is the determined cDNA sequence of clone 63299141
SEQ ID NO:3787 is the determined cDNA sequence of clone 63299142
SEQ ID NO:3788 is the determined cDNA sequence of clone 63299143
SEQ ID NO:3789 is the determined cDNA sequence of clone 63299144
SEQ ID NO:3790 is the determined cDNA sequence of clone 63299146
20 SEQ ID NO:3791 is the determined cDNA sequence of clone 63299147
SEQ ID NO:3792 is the determined cDNA sequence of clone 63299148
SEQ ID NO:3793 is the determined cDNA sequence of clone 63299152
SEQ ID NO:3794 is the determined cDNA sequence of clone 63299153
SEQ ID NO:3795 is the determined cDNA sequence of clone 63299155
25 SEQ ID NO:3796 is the determined cDNA sequence of clone 63299156
SEQ ID NO:3797 is the determined cDNA sequence of clone 63299157
SEQ ID NO:3798 is the determined cDNA sequence of clone 63299158
SEQ ID NO:3799 is the determined cDNA sequence of clone 63299159
SEQ ID NO:3800 is the determined cDNA sequence of clone 63299160
30 SEQ ID NO:3801 is the determined cDNA sequence of clone 63299164
SEQ ID NO:3802 is the determined cDNA sequence of clone 63299165

SEQ ID NO:3803 is the determined cDNA sequence of clone 63299166
SEQ ID NO:3804 is the determined cDNA sequence of clone 63298889
SEQ ID NO:3805 is the determined cDNA sequence of clone 63298890
SEQ ID NO:3806 is the determined cDNA sequence of clone 63298891
5 SEQ ID NO:3807 is the determined cDNA sequence of clone 63298892
SEQ ID NO:3808 is the determined cDNA sequence of clone 63298893
SEQ ID NO:3809 is the determined cDNA sequence of clone 63298894
SEQ ID NO:3810 is the determined cDNA sequence of clone 63298895
SEQ ID NO:3811 is the determined cDNA sequence of clone 63298896
10 SEQ ID NO:3812 is the determined cDNA sequence of clone 63298897
SEQ ID NO:3813 is the determined cDNA sequence of clone 63298898
SEQ ID NO:3814 is the determined cDNA sequence of clone 63298899
SEQ ID NO:3815 is the determined cDNA sequence of clone 63298900
SEQ ID NO:3816 is the determined cDNA sequence of clone 63298901
15 SEQ ID NO:3817 is the determined cDNA sequence of clone 63298902
SEQ ID NO:3818 is the determined cDNA sequence of clone 63298905
SEQ ID NO:3819 is the determined cDNA sequence of clone 63298906
SEQ ID NO:3820 is the determined cDNA sequence of clone 63298907
SEQ ID NO:3821 is the determined cDNA sequence of clone 63298908
20 SEQ ID NO:3822 is the determined cDNA sequence of clone 63298909
SEQ ID NO:3823 is the determined cDNA sequence of clone 63298911
SEQ ID NO:3824 is the determined cDNA sequence of clone 63298912
SEQ ID NO:3825 is the determined cDNA sequence of clone 63298913
SEQ ID NO:3826 is the determined cDNA sequence of clone 63298914
25 SEQ ID NO:3827 is the determined cDNA sequence of clone 63298915
SEQ ID NO:3828 is the determined cDNA sequence of clone 63298917
SEQ ID NO:3829 is the determined cDNA sequence of clone 63298918
SEQ ID NO:3830 is the determined cDNA sequence of clone 63298920
SEQ ID NO:3831 is the determined cDNA sequence of clone 63298921
30 SEQ ID NO:3832 is the determined cDNA sequence of clone 63298922
SEQ ID NO:3833 is the determined cDNA sequence of clone 63298923

SEQ ID NO:3834 is the determined cDNA sequence of clone 63298924
SEQ ID NO:3835 is the determined cDNA sequence of clone 63298926
SEQ ID NO:3836 is the determined cDNA sequence of clone 63298928
SEQ ID NO:3837 is the determined cDNA sequence of clone 63298930
5 SEQ ID NO:3838 is the determined cDNA sequence of clone 63298931
SEQ ID NO:3839 is the determined cDNA sequence of clone 63298932
SEQ ID NO:3840 is the determined cDNA sequence of clone 63298933
SEQ ID NO:3841 is the determined cDNA sequence of clone 63298934
SEQ ID NO:3842 is the determined cDNA sequence of clone 63298935
10 SEQ ID NO:3843 is the determined cDNA sequence of clone 63298936
SEQ ID NO:3844 is the determined cDNA sequence of clone 63298937
SEQ ID NO:3845 is the determined cDNA sequence of clone 63298938
SEQ ID NO:3846 is the determined cDNA sequence of clone 63298939
SEQ ID NO:3847 is the determined cDNA sequence of clone 63298940
15 SEQ ID NO:3848 is the determined cDNA sequence of clone 63298941
SEQ ID NO:3849 is the determined cDNA sequence of clone 63298942
SEQ ID NO:3850 is the determined cDNA sequence of clone 63298943
SEQ ID NO:3851 is the determined cDNA sequence of clone 63298944
SEQ ID NO:3852 is the determined cDNA sequence of clone 63298945
20 SEQ ID NO:3853 is the determined cDNA sequence of clone 63298946
SEQ ID NO:3854 is the determined cDNA sequence of clone 63298947
SEQ ID NO:3855 is the determined cDNA sequence of clone 63298948
SEQ ID NO:3856 is the determined cDNA sequence of clone 63298951
SEQ ID NO:3857 is the determined cDNA sequence of clone 63298952
25 SEQ ID NO:3858 is the determined cDNA sequence of clone 63298954
SEQ ID NO:3859 is the determined cDNA sequence of clone 63298957
SEQ ID NO:3860 is the determined cDNA sequence of clone 63298959
SEQ ID NO:3861 is the determined cDNA sequence of clone 63298960
SEQ ID NO:3862 is the determined cDNA sequence of clone 63298961
30 SEQ ID NO:3863 is the determined cDNA sequence of clone 63298962
SEQ ID NO:3864 is the determined cDNA sequence of clone 63298963

SEQ ID NO:3865 is the determined cDNA sequence of clone 63298964
SEQ ID NO:3866 is the determined cDNA sequence of clone 63298965
SEQ ID NO:3867 is the determined cDNA sequence of clone 63298966
SEQ ID NO:3868 is the determined cDNA sequence of clone 63298968
5 SEQ ID NO:3869 is the determined cDNA sequence of clone 63298969
SEQ ID NO:3870 is the determined cDNA sequence of clone 63298970
SEQ ID NO:3871 is the determined cDNA sequence of clone 63298971
SEQ ID NO:3872 is the determined cDNA sequence of clone 63298972
SEQ ID NO:3873 is the determined cDNA sequence of clone 63298973
10 SEQ ID NO:3874 is the determined cDNA sequence of clone 63298974
SEQ ID NO:3875 is the determined cDNA sequence of clone 63298975
SEQ ID NO:3876 is the determined cDNA sequence of clone 63298977
SEQ ID NO:3877 is the determined cDNA sequence of clone 63298978
SEQ ID NO:3878 is the determined cDNA sequence of clone 63298980
15 SEQ ID NO:3879 is the determined cDNA sequence of clone 63298330
SEQ ID NO:3880 is the determined cDNA sequence of clone 63298331
SEQ ID NO:3881 is the determined cDNA sequence of clone 63298332
SEQ ID NO:3882 is the determined cDNA sequence of clone 63298333
SEQ ID NO:3883 is the determined cDNA sequence of clone 63298334
20 SEQ ID NO:3884 is the determined cDNA sequence of clone 63298335
SEQ ID NO:3885 is the determined cDNA sequence of clone 63298336
SEQ ID NO:3886 is the determined cDNA sequence of clone 63298337
SEQ ID NO:3887 is the determined cDNA sequence of clone 63298338
SEQ ID NO:3888 is the determined cDNA sequence of clone 63298339
25 SEQ ID NO:3889 is the determined cDNA sequence of clone 63298340
SEQ ID NO:3890 is the determined cDNA sequence of clone 63298341
SEQ ID NO:3891 is the determined cDNA sequence of clone 63298342
SEQ ID NO:3892 is the determined cDNA sequence of clone 63298343
SEQ ID NO:3893 is the determined cDNA sequence of clone 63298344
30 SEQ ID NO:3894 is the determined cDNA sequence of clone 63298345
SEQ ID NO:3895 is the determined cDNA sequence of clone 63298346

SEQ ID NO:3896 is the determined cDNA sequence of clone 63298347
SEQ ID NO:3897 is the determined cDNA sequence of clone 63298348
SEQ ID NO:3898 is the determined cDNA sequence of clone 63298349
SEQ ID NO:3899 is the determined cDNA sequence of clone 63298350
5 SEQ ID NO:3900 is the determined cDNA sequence of clone 63298352
SEQ ID NO:3901 is the determined cDNA sequence of clone 63298353
SEQ ID NO:3902 is the determined cDNA sequence of clone 63298354
SEQ ID NO:3903 is the determined cDNA sequence of clone 63298355
SEQ ID NO:3904 is the determined cDNA sequence of clone 63298356
10 SEQ ID NO:3905 is the determined cDNA sequence of clone 63298358
SEQ ID NO:3906 is the determined cDNA sequence of clone 63298359
SEQ ID NO:3907 is the determined cDNA sequence of clone 63298360
SEQ ID NO:3908 is the determined cDNA sequence of clone 63298361
SEQ ID NO:3909 is the determined cDNA sequence of clone 63298363
15 SEQ ID NO:3910 is the determined cDNA sequence of clone 63298364
SEQ ID NO:3911 is the determined cDNA sequence of clone 63298365
SEQ ID NO:3912 is the determined cDNA sequence of clone 63298366
SEQ ID NO:3913 is the determined cDNA sequence of clone 63298367
SEQ ID NO:3914 is the determined cDNA sequence of clone 63298368
20 SEQ ID NO:3915 is the determined cDNA sequence of clone 63298370
SEQ ID NO:3916 is the determined cDNA sequence of clone 63298371
SEQ ID NO:3917 is the determined cDNA sequence of clone 63298372
SEQ ID NO:3918 is the determined cDNA sequence of clone 63298373
SEQ ID NO:3919 is the determined cDNA sequence of clone 63298374
25 SEQ ID NO:3920 is the determined cDNA sequence of clone 63298375
SEQ ID NO:3921 is the determined cDNA sequence of clone 63298376
SEQ ID NO:3922 is the determined cDNA sequence of clone 63298377
SEQ ID NO:3923 is the determined cDNA sequence of clone 63298378
SEQ ID NO:3924 is the determined cDNA sequence of clone 63298379
30 SEQ ID NO:3925 is the determined cDNA sequence of clone 63298380
SEQ ID NO:3926 is the determined cDNA sequence of clone 63298382

SEQ ID NO:3927 is the determined cDNA sequence of clone 63298383
SEQ ID NO:3928 is the determined cDNA sequence of clone 63298384
SEQ ID NO:3929 is the determined cDNA sequence of clone 63298385
SEQ ID NO:3930 is the determined cDNA sequence of clone 63298386
5 SEQ ID NO:3931 is the determined cDNA sequence of clone 63298387
SEQ ID NO:3932 is the determined cDNA sequence of clone 63298388
SEQ ID NO:3933 is the determined cDNA sequence of clone 63298389
SEQ ID NO:3934 is the determined cDNA sequence of clone 63298390
SEQ ID NO:3935 is the determined cDNA sequence of clone 63298391
10 SEQ ID NO:3936 is the determined cDNA sequence of clone 63298392
SEQ ID NO:3937 is the determined cDNA sequence of clone 63298394
SEQ ID NO:3938 is the determined cDNA sequence of clone 63298395
SEQ ID NO:3939 is the determined cDNA sequence of clone 63298396
SEQ ID NO:3940 is the determined cDNA sequence of clone 63298397
15 SEQ ID NO:3941 is the determined cDNA sequence of clone 63298398
SEQ ID NO:3942 is the determined cDNA sequence of clone 63298399
SEQ ID NO:3943 is the determined cDNA sequence of clone 63298401
SEQ ID NO:3944 is the determined cDNA sequence of clone 63298402
SEQ ID NO:3945 is the determined cDNA sequence of clone 63298403
20 SEQ ID NO:3946 is the determined cDNA sequence of clone 63298404
SEQ ID NO:3947 is the determined cDNA sequence of clone 63298405
SEQ ID NO:3948 is the determined cDNA sequence of clone 63298406
SEQ ID NO:3949 is the determined cDNA sequence of clone 63298407
SEQ ID NO:3950 is the determined cDNA sequence of clone 63298408
25 SEQ ID NO:3951 is the determined cDNA sequence of clone 63298409
SEQ ID NO:3952 is the determined cDNA sequence of clone 63298410
SEQ ID NO:3953 is the determined cDNA sequence of clone 63298411
SEQ ID NO:3954 is the determined cDNA sequence of clone 63298412
SEQ ID NO:3955 is the determined cDNA sequence of clone 63298414
30 SEQ ID NO:3956 is the determined cDNA sequence of clone 63298415
SEQ ID NO:3957 is the determined cDNA sequence of clone 63298416

SEQ ID NO:3958 is the determined cDNA sequence of clone 63298417
SEQ ID NO:3959 is the determined cDNA sequence of clone 63298418
SEQ ID NO:3960 is the determined cDNA sequence of clone 63298419
SEQ ID NO:3961 is the determined cDNA sequence of clone 63298420
5 SEQ ID NO:3962 is the determined cDNA sequence of clone 63298421
SEQ ID NO:3963 is the determined cDNA sequence of clone 63250604
SEQ ID NO:3964 is the determined cDNA sequence of clone 63250605
SEQ ID NO:3965 is the determined cDNA sequence of clone 63250606
SEQ ID NO:3966 is the determined cDNA sequence of clone 63250607
10 SEQ ID NO:3967 is the determined cDNA sequence of clone 63250608
SEQ ID NO:3968 is the determined cDNA sequence of clone 63250609
SEQ ID NO:3969 is the determined cDNA sequence of clone 63250610
SEQ ID NO:3970 is the determined cDNA sequence of clone 63250611
SEQ ID NO:3971 is the determined cDNA sequence of clone 63250612
15 SEQ ID NO:3972 is the determined cDNA sequence of clone 63250613
SEQ ID NO:3973 is the determined cDNA sequence of clone 63250614
SEQ ID NO:3974 is the determined cDNA sequence of clone 63250615
SEQ ID NO:3975 is the determined cDNA sequence of clone 63250616
SEQ ID NO:3976 is the determined cDNA sequence of clone 63250617
20 SEQ ID NO:3977 is the determined cDNA sequence of clone 63250618
SEQ ID NO:3978 is the determined cDNA sequence of clone 63250619
SEQ ID NO:3979 is the determined cDNA sequence of clone 63250620
SEQ ID NO:3980 is the determined cDNA sequence of clone 63250621
SEQ ID NO:3981 is the determined cDNA sequence of clone 63250622
25 SEQ ID NO:3982 is the determined cDNA sequence of clone 63250623
SEQ ID NO:3983 is the determined cDNA sequence of clone 63250624
SEQ ID NO:3984 is the determined cDNA sequence of clone 63250625
SEQ ID NO:3985 is the determined cDNA sequence of clone 63250626
SEQ ID NO:3986 is the determined cDNA sequence of clone 63250627
30 SEQ ID NO:3987 is the determined cDNA sequence of clone 63250628
SEQ ID NO:3988 is the determined cDNA sequence of clone 63250629

SEQ ID NO:3989 is the determined cDNA sequence of clone 63250630
SEQ ID NO:3990 is the determined cDNA sequence of clone 63250631
SEQ ID NO:3991 is the determined cDNA sequence of clone 63250632
SEQ ID NO:3992 is the determined cDNA sequence of clone 63250633
5 SEQ ID NO:3993 is the determined cDNA sequence of clone 63250634
SEQ ID NO:3994 is the determined cDNA sequence of clone 63250635
SEQ ID NO:3995 is the determined cDNA sequence of clone 63250636
SEQ ID NO:3996 is the determined cDNA sequence of clone 63250637
SEQ ID NO:3997 is the determined cDNA sequence of clone 63250638
10 SEQ ID NO:3998 is the determined cDNA sequence of clone 63250639
SEQ ID NO:3999 is the determined cDNA sequence of clone 63250640
SEQ ID NO:4000 is the determined cDNA sequence of clone 63250641
SEQ ID NO:4001 is the determined cDNA sequence of clone 63250642
SEQ ID NO:4002 is the determined cDNA sequence of clone 63250643
15 SEQ ID NO:4003 is the determined cDNA sequence of clone 63250644
SEQ ID NO:4004 is the determined cDNA sequence of clone 63250645
SEQ ID NO:4005 is the determined cDNA sequence of clone 63250646
SEQ ID NO:4006 is the determined cDNA sequence of clone 63250647
SEQ ID NO:4007 is the determined cDNA sequence of clone 63250648
20 SEQ ID NO:4008 is the determined cDNA sequence of clone 63250649
SEQ ID NO:4009 is the determined cDNA sequence of clone 63250650
SEQ ID NO:4010 is the determined cDNA sequence of clone 63250651
SEQ ID NO:4011 is the determined cDNA sequence of clone 63250652
SEQ ID NO:4012 is the determined cDNA sequence of clone 63250653
25 SEQ ID NO:4013 is the determined cDNA sequence of clone 63250654
SEQ ID NO:4014 is the determined cDNA sequence of clone 63250656
SEQ ID NO:4015 is the determined cDNA sequence of clone 63250657
SEQ ID NO:4016 is the determined cDNA sequence of clone 63250658
SEQ ID NO:4017 is the determined cDNA sequence of clone 63250660
30 SEQ ID NO:4018 is the determined cDNA sequence of clone 63250661
SEQ ID NO:4019 is the determined cDNA sequence of clone 63250662

SEQ ID NO:4020 is the determined cDNA sequence of clone 63250663
SEQ ID NO:4021 is the determined cDNA sequence of clone 63250664
SEQ ID NO:4022 is the determined cDNA sequence of clone 63250665
SEQ ID NO:4023 is the determined cDNA sequence of clone 63250667
5 SEQ ID NO:4024 is the determined cDNA sequence of clone 63250668
SEQ ID NO:4025 is the determined cDNA sequence of clone 63250669
SEQ ID NO:4026 is the determined cDNA sequence of clone 63250670
SEQ ID NO:4027 is the determined cDNA sequence of clone 63250671
SEQ ID NO:4028 is the determined cDNA sequence of clone 63250672
10 SEQ ID NO:4029 is the determined cDNA sequence of clone 63250673
SEQ ID NO:4030 is the determined cDNA sequence of clone 63250674
SEQ ID NO:4031 is the determined cDNA sequence of clone 63250676
SEQ ID NO:4032 is the determined cDNA sequence of clone 63250677
SEQ ID NO:4033 is the determined cDNA sequence of clone 63250678
15 SEQ ID NO:4034 is the determined cDNA sequence of clone 63250679
SEQ ID NO:4035 is the determined cDNA sequence of clone 63250681
SEQ ID NO:4036 is the determined cDNA sequence of clone 63250682
SEQ ID NO:4037 is the determined cDNA sequence of clone 63250683
SEQ ID NO:4038 is the determined cDNA sequence of clone 63250684
20 SEQ ID NO:4039 is the determined cDNA sequence of clone 63250685
SEQ ID NO:4040 is the determined cDNA sequence of clone 63250686
SEQ ID NO:4041 is the determined cDNA sequence of clone 63250687
SEQ ID NO:4042 is the determined cDNA sequence of clone 63250688
SEQ ID NO:4043 is the determined cDNA sequence of clone 63250689
25 SEQ ID NO:4044 is the determined cDNA sequence of clone 63250690
SEQ ID NO:4045 is the determined cDNA sequence of clone 63250691
SEQ ID NO:4046 is the determined cDNA sequence of clone 63250692
SEQ ID NO:4047 is the determined cDNA sequence of clone 63250693
SEQ ID NO:4048 is the determined cDNA sequence of clone 63250694
30 SEQ ID NO:4049 is the determined cDNA sequence of clone 63250696
SEQ ID NO:4050 is the determined cDNA sequence of clone 63138129

SEQ ID NO:4051 is the determined cDNA sequence of clone 63138130
SEQ ID NO:4052 is the determined cDNA sequence of clone 63138131
SEQ ID NO:4053 is the determined cDNA sequence of clone 63138132
SEQ ID NO:4054 is the determined cDNA sequence of clone 63138133
5 SEQ ID NO:4055 is the determined cDNA sequence of clone 63138134
SEQ ID NO:4056 is the determined cDNA sequence of clone 63138135
SEQ ID NO:4057 is the determined cDNA sequence of clone 63138136
SEQ ID NO:4058 is the determined cDNA sequence of clone 63138137
SEQ ID NO:4059 is the determined cDNA sequence of clone 63138138
10 SEQ ID NO:4060 is the determined cDNA sequence of clone 63138139
SEQ ID NO:4061 is the determined cDNA sequence of clone 63138140
SEQ ID NO:4062 is the determined cDNA sequence of clone 63138141
SEQ ID NO:4063 is the determined cDNA sequence of clone 63138142
SEQ ID NO:4064 is the determined cDNA sequence of clone 63138144
15 SEQ ID NO:4065 is the determined cDNA sequence of clone 63138145
SEQ ID NO:4066 is the determined cDNA sequence of clone 63138146
SEQ ID NO:4067 is the determined cDNA sequence of clone 63138147
SEQ ID NO:4068 is the determined cDNA sequence of clone 63138148
SEQ ID NO:4069 is the determined cDNA sequence of clone 63138149
20 SEQ ID NO:4070 is the determined cDNA sequence of clone 63138150
SEQ ID NO:4071 is the determined cDNA sequence of clone 63138151
SEQ ID NO:4072 is the determined cDNA sequence of clone 63138153
SEQ ID NO:4073 is the determined cDNA sequence of clone 63138154
SEQ ID NO:4074 is the determined cDNA sequence of clone 63138155
25 SEQ ID NO:4075 is the determined cDNA sequence of clone 63138156
SEQ ID NO:4076 is the determined cDNA sequence of clone 63138157
SEQ ID NO:4077 is the determined cDNA sequence of clone 63138158
SEQ ID NO:4078 is the determined cDNA sequence of clone 63138159
SEQ ID NO:4079 is the determined cDNA sequence of clone 63138161
30 SEQ ID NO:4080 is the determined cDNA sequence of clone 63138162
SEQ ID NO:4081 is the determined cDNA sequence of clone 63138163

SEQ ID NO:4082 is the determined cDNA sequence of clone 63138165
SEQ ID NO:4083 is the determined cDNA sequence of clone 63138166
SEQ ID NO:4084 is the determined cDNA sequence of clone 63138167
SEQ ID NO:4085 is the determined cDNA sequence of clone 63138169
5 SEQ ID NO:4086 is the determined cDNA sequence of clone 63138170
SEQ ID NO:4087 is the determined cDNA sequence of clone 63138171
SEQ ID NO:4088 is the determined cDNA sequence of clone 63138172
SEQ ID NO:4089 is the determined cDNA sequence of clone 63138173
SEQ ID NO:4090 is the determined cDNA sequence of clone 63138174
10 SEQ ID NO:4091 is the determined cDNA sequence of clone 63138175
SEQ ID NO:4092 is the determined cDNA sequence of clone 63138176
SEQ ID NO:4093 is the determined cDNA sequence of clone 63138177
SEQ ID NO:4094 is the determined cDNA sequence of clone 63138178
SEQ ID NO:4095 is the determined cDNA sequence of clone 63138179
15 SEQ ID NO:4096 is the determined cDNA sequence of clone 63138181
SEQ ID NO:4097 is the determined cDNA sequence of clone 63138182
SEQ ID NO:4098 is the determined cDNA sequence of clone 63138183
SEQ ID NO:4099 is the determined cDNA sequence of clone 63138184
SEQ ID NO:4100 is the determined cDNA sequence of clone 63138185
20 SEQ ID NO:4101 is the determined cDNA sequence of clone 63138186
SEQ ID NO:4102 is the determined cDNA sequence of clone 63138187
SEQ ID NO:4103 is the determined cDNA sequence of clone 63138189
SEQ ID NO:4104 is the determined cDNA sequence of clone 63138191
SEQ ID NO:4105 is the determined cDNA sequence of clone 63138192
25 SEQ ID NO:4106 is the determined cDNA sequence of clone 63138193
SEQ ID NO:4107 is the determined cDNA sequence of clone 63138194
SEQ ID NO:4108 is the determined cDNA sequence of clone 63138195
SEQ ID NO:4109 is the determined cDNA sequence of clone 63138196
SEQ ID NO:4110 is the determined cDNA sequence of clone 63138197
30 SEQ ID NO:4111 is the determined cDNA sequence of clone 63138198
SEQ ID NO:4112 is the determined cDNA sequence of clone 63138199

SEQ ID NO:4113 is the determined cDNA sequence of clone 63138201
SEQ ID NO:4114 is the determined cDNA sequence of clone 63138202
SEQ ID NO:4115 is the determined cDNA sequence of clone 63138203
SEQ ID NO:4116 is the determined cDNA sequence of clone 63138204
5 SEQ ID NO:4117 is the determined cDNA sequence of clone 63138205
SEQ ID NO:4118 is the determined cDNA sequence of clone 63138206
SEQ ID NO:4119 is the determined cDNA sequence of clone 63138208
SEQ ID NO:4120 is the determined cDNA sequence of clone 63138209
SEQ ID NO:4121 is the determined cDNA sequence of clone 63138210
10 SEQ ID NO:4122 is the determined cDNA sequence of clone 63138211
SEQ ID NO:4123 is the determined cDNA sequence of clone 63138212
SEQ ID NO:4124 is the determined cDNA sequence of clone 63138213
SEQ ID NO:4125 is the determined cDNA sequence of clone 63138214
SEQ ID NO:4126 is the determined cDNA sequence of clone 63138215
15 SEQ ID NO:4127 is the determined cDNA sequence of clone 63138217
SEQ ID NO:4128 is the determined cDNA sequence of clone 63138218
SEQ ID NO:4129 is the determined cDNA sequence of clone 63138220
SEQ ID NO:4130 is the determined cDNA sequence of clone 63138221
SEQ ID NO:4131 is the determined cDNA sequence of clone 63299167
20 SEQ ID NO:4132 is the determined cDNA sequence of clone 63299168
SEQ ID NO:4133 is the determined cDNA sequence of clone 63299169
SEQ ID NO:4134 is the determined cDNA sequence of clone 63299171
SEQ ID NO:4135 is the determined cDNA sequence of clone 63299172
SEQ ID NO:4136 is the determined cDNA sequence of clone 63299173
25 SEQ ID NO:4137 is the determined cDNA sequence of clone 63299174
SEQ ID NO:4138 is the determined cDNA sequence of clone 63299175
SEQ ID NO:4139 is the determined cDNA sequence of clone 63299176
SEQ ID NO:4140 is the determined cDNA sequence of clone 63299177
SEQ ID NO:4141 is the determined cDNA sequence of clone 63299178
30 SEQ ID NO:4142 is the determined cDNA sequence of clone 63299179
SEQ ID NO:4143 is the determined cDNA sequence of clone 63299180

SEQ ID NO:4144 is the determined cDNA sequence of clone 63299181
SEQ ID NO:4145 is the determined cDNA sequence of clone 63299182
SEQ ID NO:4146 is the determined cDNA sequence of clone 63299183
SEQ ID NO:4147 is the determined cDNA sequence of clone 63299185
5 SEQ ID NO:4148 is the determined cDNA sequence of clone 63299187
SEQ ID NO:4149 is the determined cDNA sequence of clone 63299188
SEQ ID NO:4150 is the determined cDNA sequence of clone 63299189
SEQ ID NO:4151 is the determined cDNA sequence of clone 63299191
SEQ ID NO:4152 is the determined cDNA sequence of clone 63299193
10 SEQ ID NO:4153 is the determined cDNA sequence of clone 63299194
SEQ ID NO:4154 is the determined cDNA sequence of clone 63299195
SEQ ID NO:4155 is the determined cDNA sequence of clone 63299197
SEQ ID NO:4156 is the determined cDNA sequence of clone 63299198
SEQ ID NO:4157 is the determined cDNA sequence of clone 63299199
15 SEQ ID NO:4158 is the determined cDNA sequence of clone 63299200
SEQ ID NO:4159 is the determined cDNA sequence of clone 63299201
SEQ ID NO:4160 is the determined cDNA sequence of clone 63299203
SEQ ID NO:4161 is the determined cDNA sequence of clone 63299204
SEQ ID NO:4162 is the determined cDNA sequence of clone 63299206
20 SEQ ID NO:4163 is the determined cDNA sequence of clone 63299209
SEQ ID NO:4164 is the determined cDNA sequence of clone 63299210
SEQ ID NO:4165 is the determined cDNA sequence of clone 63299211
SEQ ID NO:4166 is the determined cDNA sequence of clone 63299212
SEQ ID NO:4167 is the determined cDNA sequence of clone 63299213
25 SEQ ID NO:4168 is the determined cDNA sequence of clone 63299214
SEQ ID NO:4169 is the determined cDNA sequence of clone 63299215
SEQ ID NO:4170 is the determined cDNA sequence of clone 63299216
SEQ ID NO:4171 is the determined cDNA sequence of clone 63299217
SEQ ID NO:4172 is the determined cDNA sequence of clone 63299218
30 SEQ ID NO:4173 is the determined cDNA sequence of clone 63299221
SEQ ID NO:4174 is the determined cDNA sequence of clone 63299222

SEQ ID NO:4175 is the determined cDNA sequence of clone 63299223
SEQ ID NO:4176 is the determined cDNA sequence of clone 63299224
SEQ ID NO:4177 is the determined cDNA sequence of clone 63299226
SEQ ID NO:4178 is the determined cDNA sequence of clone 63299227
5 SEQ ID NO:4179 is the determined cDNA sequence of clone 63299228
SEQ ID NO:4180 is the determined cDNA sequence of clone 63299229
SEQ ID NO:4181 is the determined cDNA sequence of clone 63299230
SEQ ID NO:4182 is the determined cDNA sequence of clone 63299231
SEQ ID NO:4183 is the determined cDNA sequence of clone 63299233
10 SEQ ID NO:4184 is the determined cDNA sequence of clone 63299235
SEQ ID NO:4185 is the determined cDNA sequence of clone 63299236
SEQ ID NO:4186 is the determined cDNA sequence of clone 63299237
SEQ ID NO:4187 is the determined cDNA sequence of clone 63299239
SEQ ID NO:4188 is the determined cDNA sequence of clone 63299240
15 SEQ ID NO:4189 is the determined cDNA sequence of clone 63299242
SEQ ID NO:4190 is the determined cDNA sequence of clone 63299243
SEQ ID NO:4191 is the determined cDNA sequence of clone 63299245
SEQ ID NO:4192 is the determined cDNA sequence of clone 63299247
SEQ ID NO:4193 is the determined cDNA sequence of clone 63299248
20 SEQ ID NO:4194 is the determined cDNA sequence of clone 63299249
SEQ ID NO:4195 is the determined cDNA sequence of clone 63299250
SEQ ID NO:4196 is the determined cDNA sequence of clone 63299251
SEQ ID NO:4197 is the determined cDNA sequence of clone 63299252
SEQ ID NO:4198 is the determined cDNA sequence of clone 63299253
25 SEQ ID NO:4199 is the determined cDNA sequence of clone 63299254
SEQ ID NO:4200 is the determined cDNA sequence of clone 63299256
SEQ ID NO:4201 is the determined cDNA sequence of clone 63299257
SEQ ID NO:4202 is the determined cDNA sequence of clone 63299259
SEQ ID NO:4203 is the determined cDNA sequence of clone 63234997
30 SEQ ID NO:4204 is the determined cDNA sequence of clone 63234998
SEQ ID NO:4205 is the determined cDNA sequence of clone 63234999

SEQ ID NO:4206 is the determined cDNA sequence of clone 63235000
SEQ ID NO:4207 is the determined cDNA sequence of clone 63235001
SEQ ID NO:4208 is the determined cDNA sequence of clone 63235002
SEQ ID NO:4209 is the determined cDNA sequence of clone 63235003
5 SEQ ID NO:4210 is the determined cDNA sequence of clone 63235004
SEQ ID NO:4211 is the determined cDNA sequence of clone 63235007
SEQ ID NO:4212 is the determined cDNA sequence of clone 63235008
SEQ ID NO:4213 is the determined cDNA sequence of clone 63235009
SEQ ID NO:4214 is the determined cDNA sequence of clone 63235011
10 SEQ ID NO:4215 is the determined cDNA sequence of clone 63235012
SEQ ID NO:4216 is the determined cDNA sequence of clone 63235014
SEQ ID NO:4217 is the determined cDNA sequence of clone 63235015
SEQ ID NO:4218 is the determined cDNA sequence of clone 63235016
SEQ ID NO:4219 is the determined cDNA sequence of clone 63235019
15 SEQ ID NO:4220 is the determined cDNA sequence of clone 63235020
SEQ ID NO:4221 is the determined cDNA sequence of clone 63235021
SEQ ID NO:4222 is the determined cDNA sequence of clone 63235022
SEQ ID NO:4223 is the determined cDNA sequence of clone 63235023
SEQ ID NO:4224 is the determined cDNA sequence of clone 63235024
20 SEQ ID NO:4225 is the determined cDNA sequence of clone 63235025
SEQ ID NO:4226 is the determined cDNA sequence of clone 63235028
SEQ ID NO:4227 is the determined cDNA sequence of clone 63235029
SEQ ID NO:4228 is the determined cDNA sequence of clone 63235031
SEQ ID NO:4229 is the determined cDNA sequence of clone 63235033
25 SEQ ID NO:4230 is the determined cDNA sequence of clone 63235034
SEQ ID NO:4231 is the determined cDNA sequence of clone 63235037
SEQ ID NO:4232 is the determined cDNA sequence of clone 63235038
SEQ ID NO:4233 is the determined cDNA sequence of clone 63235039
SEQ ID NO:4234 is the determined cDNA sequence of clone 63235043
30 SEQ ID NO:4235 is the determined cDNA sequence of clone 63235044
SEQ ID NO:4236 is the determined cDNA sequence of clone 63235045

SEQ ID NO:4237 is the determined cDNA sequence of clone 63235046
SEQ ID NO:4238 is the determined cDNA sequence of clone 63235047
SEQ ID NO:4239 is the determined cDNA sequence of clone 63235048
SEQ ID NO:4240 is the determined cDNA sequence of clone 63235049
5 SEQ ID NO:4241 is the determined cDNA sequence of clone 63235050
SEQ ID NO:4242 is the determined cDNA sequence of clone 63235051
SEQ ID NO:4243 is the determined cDNA sequence of clone 63235052
SEQ ID NO:4244 is the determined cDNA sequence of clone 63235053
SEQ ID NO:4245 is the determined cDNA sequence of clone 63235056
10 SEQ ID NO:4246 is the determined cDNA sequence of clone 63235057
SEQ ID NO:4247 is the determined cDNA sequence of clone 63235058
SEQ ID NO:4248 is the determined cDNA sequence of clone 63235059
SEQ ID NO:4249 is the determined cDNA sequence of clone 63235060
SEQ ID NO:4250 is the determined cDNA sequence of clone 63235061
15 SEQ ID NO:4251 is the determined cDNA sequence of clone 63235062
SEQ ID NO:4252 is the determined cDNA sequence of clone 63235063
SEQ ID NO:4253 is the determined cDNA sequence of clone 63235064
SEQ ID NO:4254 is the determined cDNA sequence of clone 63235067
SEQ ID NO:4255 is the determined cDNA sequence of clone 63235068
20 SEQ ID NO:4256 is the determined cDNA sequence of clone 63235069
SEQ ID NO:4257 is the determined cDNA sequence of clone 63235070
SEQ ID NO:4258 is the determined cDNA sequence of clone 63235071
SEQ ID NO:4259 is the determined cDNA sequence of clone 63235072
SEQ ID NO:4260 is the determined cDNA sequence of clone 63235073
25 SEQ ID NO:4261 is the determined cDNA sequence of clone 63235074
SEQ ID NO:4262 is the determined cDNA sequence of clone 63235075
SEQ ID NO:4263 is the determined cDNA sequence of clone 63235077
SEQ ID NO:4264 is the determined cDNA sequence of clone 63235078
SEQ ID NO:4265 is the determined cDNA sequence of clone 63235079
30 SEQ ID NO:4266 is the determined cDNA sequence of clone 63235080
SEQ ID NO:4267 is the determined cDNA sequence of clone 63235081

SEQ ID NO:4268 is the determined cDNA sequence of clone 63235082
SEQ ID NO:4269 is the determined cDNA sequence of clone 63235084
SEQ ID NO:4270 is the determined cDNA sequence of clone 63235085
SEQ ID NO:4271 is the determined cDNA sequence of clone 63235086
5 SEQ ID NO:4272 is the determined cDNA sequence of clone 63235087
SEQ ID NO:4273 is the determined cDNA sequence of clone 63792101
SEQ ID NO:4274 is the determined cDNA sequence of clone 63792102
SEQ ID NO:4275 is the determined cDNA sequence of clone 63792103
SEQ ID NO:4276 is the determined cDNA sequence of clone 63792104
10 SEQ ID NO:4277 is the determined cDNA sequence of clone 63792105
SEQ ID NO:4278 is the determined cDNA sequence of clone 63792106
SEQ ID NO:4279 is the determined cDNA sequence of clone 63792107
SEQ ID NO:4280 is the determined cDNA sequence of clone 63792108
SEQ ID NO:4281 is the determined cDNA sequence of clone 63792109
15 SEQ ID NO:4282 is the determined cDNA sequence of clone 63792110
SEQ ID NO:4283 is the determined cDNA sequence of clone 63792114
SEQ ID NO:4284 is the determined cDNA sequence of clone 63792115
SEQ ID NO:4285 is the determined cDNA sequence of clone 63792116
SEQ ID NO:4286 is the determined cDNA sequence of clone 63792117
20 SEQ ID NO:4287 is the determined cDNA sequence of clone 63792118
SEQ ID NO:4288 is the determined cDNA sequence of clone 63792119
SEQ ID NO:4289 is the determined cDNA sequence of clone 63792120
SEQ ID NO:4290 is the determined cDNA sequence of clone 63792121
SEQ ID NO:4291 is the determined cDNA sequence of clone 63792124
25 SEQ ID NO:4292 is the determined cDNA sequence of clone 63792125
SEQ ID NO:4293 is the determined cDNA sequence of clone 63792127
SEQ ID NO:4294 is the determined cDNA sequence of clone 63792128
SEQ ID NO:4295 is the determined cDNA sequence of clone 63792129
SEQ ID NO:4296 is the determined cDNA sequence of clone 63792130
30 SEQ ID NO:4297 is the determined cDNA sequence of clone 63792131
SEQ ID NO:4298 is the determined cDNA sequence of clone 63792132

SEQ ID NO:4299 is the determined cDNA sequence of clone 63792136
SEQ ID NO:4300 is the determined cDNA sequence of clone 63792137
SEQ ID NO:4301 is the determined cDNA sequence of clone 63792138
SEQ ID NO:4302 is the determined cDNA sequence of clone 63792139
5 SEQ ID NO:4303 is the determined cDNA sequence of clone 63792140
SEQ ID NO:4304 is the determined cDNA sequence of clone 63792141
SEQ ID NO:4305 is the determined cDNA sequence of clone 63792144
SEQ ID NO:4306 is the determined cDNA sequence of clone 63792145
SEQ ID NO:4307 is the determined cDNA sequence of clone 63792146
10 SEQ ID NO:4308 is the determined cDNA sequence of clone 63792149
SEQ ID NO:4309 is the determined cDNA sequence of clone 63792150
SEQ ID NO:4310 is the determined cDNA sequence of clone 63792151
SEQ ID NO:4311 is the determined cDNA sequence of clone 63792152
SEQ ID NO:4312 is the determined cDNA sequence of clone 63792153
15 SEQ ID NO:4313 is the determined cDNA sequence of clone 63792156
SEQ ID NO:4314 is the determined cDNA sequence of clone 63792157
SEQ ID NO:4315 is the determined cDNA sequence of clone 63792159
SEQ ID NO:4316 is the determined cDNA sequence of clone 63792160
SEQ ID NO:4317 is the determined cDNA sequence of clone 63792161
20 SEQ ID NO:4318 is the determined cDNA sequence of clone 63792162
SEQ ID NO:4319 is the determined cDNA sequence of clone 63792163
SEQ ID NO:4320 is the determined cDNA sequence of clone 63792165
SEQ ID NO:4321 is the determined cDNA sequence of clone 63792166
SEQ ID NO:4322 is the determined cDNA sequence of clone 63792167
25 SEQ ID NO:4323 is the determined cDNA sequence of clone 63792168
SEQ ID NO:4324 is the determined cDNA sequence of clone 63792169
SEQ ID NO:4325 is the determined cDNA sequence of clone 63792170
SEQ ID NO:4326 is the determined cDNA sequence of clone 63792171
SEQ ID NO:4327 is the determined cDNA sequence of clone 63792172
30 SEQ ID NO:4328 is the determined cDNA sequence of clone 63792173
SEQ ID NO:4329 is the determined cDNA sequence of clone 63792174

SEQ ID NO:4330 is the determined cDNA sequence of clone 63792175
SEQ ID NO:4331 is the determined cDNA sequence of clone 63792176
SEQ ID NO:4332 is the determined cDNA sequence of clone 63792177
SEQ ID NO:4333 is the determined cDNA sequence of clone 63792178
5 SEQ ID NO:4334 is the determined cDNA sequence of clone 63792179
SEQ ID NO:4335 is the determined cDNA sequence of clone 63792180
SEQ ID NO:4336 is the determined cDNA sequence of clone 63792181
SEQ ID NO:4337 is the determined cDNA sequence of clone 63792183
SEQ ID NO:4338 is the determined cDNA sequence of clone 63792184
10 SEQ ID NO:4339 is the determined cDNA sequence of clone 63792185
SEQ ID NO:4340 is the determined cDNA sequence of clone 63792186
SEQ ID NO:4341 is the determined cDNA sequence of clone 63792187
SEQ ID NO:4342 is the determined cDNA sequence of clone 63792188
SEQ ID NO:4343 is the determined cDNA sequence of clone 63792189
15 SEQ ID NO:4344 is the determined cDNA sequence of clone 63792190
SEQ ID NO:4345 is the determined cDNA sequence of clone 63792192
SEQ ID NO:4346 is the determined cDNA sequence of clone
p0150r10c11
SEQ ID NO:4347 is the determined cDNA sequence of clone
20 p0150r07c17
SEQ ID NO:4348 is the determined cDNA sequence of clone
p0150r09c15
SEQ ID NO:4349 is the determined cDNA sequence of clone
p0150r07c14
25 SEQ ID NO:4350 is the determined cDNA sequence of clone
p0150r11c05
SEQ ID NO:4351 is the determined cDNA sequence of clone
p0160r06c18
SEQ ID NO:4352 is the determined cDNA sequence of clone
30 p0160r02c21

SEQ ID NO:4353 is the determined cDNA sequence of clone
p0160r13c02

SEQ ID NO:4354 is the determined cDNA sequence of clone
p0150r13c04

5 SEQ ID NO:4355 is the determined cDNA sequence of clone
p0150r02c15

SEQ ID NO:4356 is the determined cDNA sequence of clone
p0150r06c12

10 SEQ ID NO:4357 is the determined cDNA sequence of clone
p0151r06c12

SEQ ID NO:4358 is the determined cDNA sequence of clone
p0150r14c04

15 SEQ ID NO:4359 is the determined cDNA sequence of clone
p0150r02c06

15 SEQ ID NO:4360 is the determined cDNA sequence of clone
p0150r04c19

15 SEQ ID NO:4361 is the determined cDNA sequence of clone
p0150r03c18

20 SEQ ID NO:4362 is the determined cDNA sequence of clone
p0151rl3c03

20 SEQ ID NO:4363 is the determined cDNA sequence of clone
p0150r01c08

20 SEQ ID NO:4364 is the determined cDNA sequence of clone
p0150r11c07

25 SEQ ID NO:4365 is the determined cDNA sequence of clone
p0150r02c11

25 SEQ ID NO:4366 is the determined cDNA sequence of clone
p0150r01c17

25 SEQ ID NO:4367 is the determined cDNA sequence of clone
30 p0150r05c16

SEQ ID NO:4368 is the determined cDNA sequence of clone
p0150r06c04

SEQ ID NO:4369 is the determined cDNA sequence of clone
p0150r15c17

5 SEQ ID NO:4370 is the determined cDNA sequence of clone
p0150r15c11

 SEQ ID NO:4371 is the determined cDNA sequence of clone
p0150r09c13

 SEQ ID NO:4372 is the determined cDNA sequence of clone
10 p0150r13c03

 SEQ ID NO:4373 is the determined cDNA sequence of clone
p0150r09c10

 SEQ ID NO:4374 is the determined cDNA sequence of clone
p0161r13c17

15 SEQ ID NO:4375 is the determined cDNA sequence of clone
p0159r16c21

 SEQ ID NO:4376 is the determined cDNA sequence of clone
p0150r02c02

 SEQ ID NO:4377 is the determined cDNA sequence of clone
20 p0151r09c19

 SEQ ID NO:4378 is the determined cDNA sequence of clone
p0151r02c06

 SEQ ID NO:4379 is the determined cDNA sequence of clone
p0150r16c06

25 SEQ ID NO:4380 is the determined cDNA sequence of clone
p0150r09c12

 SEQ ID NO:4381 is the determined cDNA sequence of clone
p0150r07c06

 SEQ ID NO:4382 is the determined cDNA sequence of clone
30 p0150r06c19

SEQ ID NO:4383 is the determined cDNA sequence of clone
p0150r04c05

SEQ ID NO:4384 is the determined cDNA sequence of clone
p0150r03c21

5 SEQ ID NO:4385 is the determined cDNA sequence of clone
p0150r02c18

SEQ ID NO:4386 is the determined cDNA sequence of clone
p0150r15c07

10 SEQ ID NO:4387 is the determined cDNA sequence of clone
p0150r10c15

SEQ ID NO:4388 is the determined cDNA sequence of clone
p0150r07c05

15 SEQ ID NO:4389 is the determined cDNA sequence of clone
p0150r06c08

SEQ ID NO:4390 is the determined cDNA sequence of clone
p0150r01c24

20 SEQ ID NO:4391 is the determined cDNA sequence of clone
p0150r07c15

SEQ ID NO:4392 is the determined cDNA sequence of clone
p0150r02c23

25 SEQ ID NO:4393 is the determined cDNA sequence of clone
p0151r09c08

SEQ ID NO:4394 is the determined cDNA sequence of clone
p0150r16c09

30 SEQ ID NO:4395 is the determined cDNA sequence of clone
p0150r14c11

SEQ ID NO:4396 is the determined cDNA sequence of clone
p0151r05c12

SEQ ID NO:4397 is the determined cDNA sequence of clone
p0150r12c23

SEQ ID NO:4398 is the determined cDNA sequence of clone
p0150r16c02

SEQ ID NO:4399 is the determined cDNA sequence of clone
p0155r10c08

5 SEQ ID NO:4400 is the determined cDNA sequence of clone
p0150r02c05

SEQ ID NO:4401 is the determined cDNA sequence of clone
p0150r09c04

SEQ ID NO:4402 is the determined cDNA sequence of clone
10 p0150r03c22

SEQ ID NO:4403 is the determined cDNA sequence of clone
p0150r15c10

SEQ ID NO:4404 is the determined cDNA sequence of clone
p0150r13c20

15 SEQ ID NO:4405 is the determined cDNA sequence of clone
p0150r08c18

SEQ ID NO:4406 is the determined cDNA sequence of clone
p0150r09c22

SEQ ID NO:4407 is the determined cDNA sequence of clone
20 p0157r08c09

SEQ ID NO:4408 is the determined cDNA sequence of clone
p0163r04c09

SEQ ID NO:4409 is the determined cDNA sequence of clone
p0155r01c04

25 SEQ ID NO:4410 is the determined cDNA sequence of clone
p0152r16c22

SEQ ID NO:4411 is the determined cDNA sequence of clone
p0152r16c12

SEQ ID NO:4412 is the determined cDNA sequence of clone
30 p0150r01c16

SEQ ID NO:4413 is the determined cDNA sequence of clone
p0150r05c23

SEQ ID NO:4414 is the determined cDNA sequence of clone
p0150r11c09

5 SEQ ID NO:4415 is the determined cDNA sequence of clone
p0150r13c22

 SEQ ID NO:4416 is the determined cDNA sequence of clone
p0150r11c17

 SEQ ID NO:4417 is the determined cDNA sequence of clone
10 p0159r16c01

 SEQ ID NO:4418 is the determined cDNA sequence of clone
p0156r16c21

 SEQ ID NO:4419 is the determined cDNA sequence of clone
p0150r06c15

15 SEQ ID NO:4420 is the determined cDNA sequence of clone
p0151r05c04

 SEQ ID NO:4421 is the determined cDNA sequence of clone
p0150r05c21

 SEQ ID NO:4422 is the determined cDNA sequence of clone
20 p0150r11c22

 SEQ ID NO:4423 is the determined cDNA sequence of clone
p0150r01c14

 SEQ ID NO:4424 is the determined cDNA sequence of clone
p0150r15c08

25 SEQ ID NO:4425 is the determined cDNA sequence of clone
p0150r11c02

 SEQ ID NO:4426 is the determined cDNA sequence of clone
p0157r07c21

 SEQ ID NO:4427 is the determined cDNA sequence of clone
30 p0150r16c17

SEQ ID NO:4428 is the determined cDNA sequence of clone
p0155r03c08

SEQ ID NO:4429 is the determined cDNA sequence of clone
p0150r07c10

5 SEQ ID NO:4430 is the determined cDNA sequence of clone
p0150r16c13

SEQ ID NO:4431 is the determined cDNA sequence of clone
p0150r06c10

10 SEQ ID NO:4432 is the determined cDNA sequence of clone
p0150r02c16

. SEQ ID NO:4433 is the determined cDNA sequence of clone
p0150r09c06

 SEQ ID NO:4434 is the determined cDNA sequence of clone
p0150r11c16

15 SEQ ID NO:4435 is the determined cDNA sequence of clone
p0150r01c13

 SEQ ID NO:4436 is the determined cDNA sequence of clone
p0150r08c10

 SEQ ID NO:4437 is the determined cDNA sequence of clone
20 p0150r05c18

 SEQ ID NO:4438 is the determined cDNA sequence of clone
p0159r14c18

 SEQ ID NO:4439 is the determined cDNA sequence of clone
p0150r16c22

25 SEQ ID NO:4440 is the determined cDNA sequence of clone
p0152r10c20

 SEQ ID NO:4441 is the determined cDNA sequence of clone
p0150r13c23

 SEQ ID NO:4442 is the determined cDNA sequence of clone
30 p0150r12c10

SEQ ID NO:4443 is the determined cDNA sequence of clone
p0150r09c18

SEQ ID NO:4444 is the determined cDNA sequence of clone
p0158r09c04

5 SEQ ID NO:4445 is the determined cDNA sequence of clone
p0150r08c09

 SEQ ID NO:4446 is the determined cDNA sequence of clone
p0150r11c11

10 SEQ ID NO:4447 is the determined cDNA sequence of clone
p0150r15c01

 SEQ ID NO:4448 is the determined cDNA sequence of clone
p0157r07c01

 SEQ ID NO:4449 is the determined cDNA sequence of clone
p0150r09c21

15 SEQ ID NO:4450 is the determined cDNA sequence of clone
p0150r12c02

 SEQ ID NO:4451 is the determined cDNA sequence of clone
p0150r03c17

 SEQ ID NO:4452 is the determined cDNA sequence of clone
20 p0157r07c20

 SEQ ID NO:4453 is the determined cDNA sequence of clone
p0150r05c20

 SEQ ID NO:4454 is the determined cDNA sequence of clone
p0150r05c04

25 SEQ ID NO:4455 is the determined cDNA sequence of clone
p0150r07c12

 SEQ ID NO:4456 is the determined cDNA sequence of clone
p0150r05c02

 SEQ ID NO:4457 is the determined cDNA sequence of clone
30 p0152r13c24

SEQ ID NO:4458 is the determined cDNA sequence of clone
p0150r03c11

SEQ ID NO:4459 is the determined cDNA sequence of clone
p0162r13c11

5 SEQ ID NO:4460 is the determined cDNA sequence of clone
p0151r13c15

 SEQ ID NO:4461 is the determined cDNA sequence of clone
p0150r03c01

 SEQ ID NO:4462 is the determined cDNA sequence of clone
10 p0151r08c17

 SEQ ID NO:4463 is the determined cDNA sequence of clone
p0150r01c02

 SEQ ID NO:4464 is the determined cDNA sequence of clone
p0150r04c06

15 SEQ ID NO:4465 is the determined cDNA sequence of clone
p0150r09c19

 SEQ ID NO:4466 is the determined cDNA sequence of clone
p0153r06c10

 SEQ ID NO:4467 is the determined cDNA sequence of clone
20 p0150r02c20

 SEQ ID NO:4468 is the determined cDNA sequence of clone
p0155r09c08

 SEQ ID NO:4469 is the determined cDNA sequence of clone
p0152r16c01

25 SEQ ID NO:4470 is the determined cDNA sequence of clone
p0150r13c02

 SEQ ID NO:4471 is the determined cDNA sequence of clone
p0150r12c22

 SEQ ID NO:4472 is the determined cDNA sequence of clone
30 p0150r11c23

SEQ ID NO:4473 is the determined cDNA sequence of clone
p0155r10c24

SEQ ID NO:4474 is the determined cDNA sequence of clone
p0157r06c03

5 SEQ ID NO:4475 is the determined cDNA sequence of clone
p0150r05c24

SEQ ID NO:4476 is the determined cDNA sequence of clone
p0150r11c04

10 SEQ ID NO:4477 is the determined cDNA sequence of clone
p0156r16c18

SEQ ID NO:4478 is the determined cDNA sequence of clone
p0155r10c19

15 SEQ ID NO:4479 is the determined cDNA sequence of clone
p0150r14c23

15 SEQ ID NO:4480 is the determined cDNA sequence of clone
p0150r10c19

15 SEQ ID NO:4481 is the determined cDNA sequence of clone
p0150r11c19

20 SEQ ID NO:4482 is the determined cDNA sequence of clone
p0150r15c21

SEQ ID NO:4483 is the determined cDNA sequence of clone
p0150r11c21

20 SEQ ID NO:4484 is the determined cDNA sequence of clone
p0157r05c22

25 SEQ ID NO:4485 is the determined cDNA sequence of clone
p0157r05c21

25 SEQ ID NO:4486 is the determined cDNA sequence of clone
p0157r06c05

30 SEQ ID NO:4487 is the determined cDNA sequence of clone
p0157r06c05

SEQ ID NO:4488 is the determined cDNA sequence of clone
p0150r15c22

SEQ ID NO:4489 is the determined cDNA sequence of clone
p0150r03c13

5 SEQ ID NO:4490 is the determined cDNA sequence of clone
p0160r04c18

SEQ ID NO:4491 is the determined cDNA sequence of clone
p0150r06c23

10 SEQ ID NO:4492 is the determined cDNA sequence of clone
p0150r02c15

SEQ ID NO:4493 is the determined cDNA sequence of clone
p0150r13c24

15 SEQ ID NO:4494 is the determined cDNA sequence of clone
p0150r15c03

15 SEQ ID NO:4495 is the determined cDNA sequence of clone
p0150r05c19

15 SEQ ID NO:4496 is the determined cDNA sequence of clone
p0150r07c01

20 SEQ ID NO:4497 is the determined cDNA sequence of clone
p0150r06c16

SEQ ID NO:4498 is the determined cDNA sequence of clone
p0150r02c07

20 SEQ ID NO:4499 is the determined cDNA sequence of clone
p0152r15c23

25 SEQ ID NO:4500 is the determined cDNA sequence of clone
p0150r11c01

25 SEQ ID NO:4501 is the determined cDNA sequence of clone
p0150r03c14

30 SEQ ID NO:4502 is the determined cDNA sequence of clone
p0150r02c12

SEQ ID NO:4503 is the determined cDNA sequence of clone
p0150r04c17

SEQ ID NO:4504 is the determined cDNA sequence of clone
p0150r01c04

5 SEQ ID NO:4505 is the determined cDNA sequence of clone
p0150r02c22

 SEQ ID NO:4506 is the determined cDNA sequence of clone
p0150r09c01

10 SEQ ID NO:4507 is the determined cDNA sequence of clone
p0150r08c17

 SEQ ID NO:4508 is the determined cDNA sequence of clone
p0150r09c17

 SEQ ID NO:4509 is the determined cDNA sequence of clone
p0150r09c20

15 SEQ ID NO:4510 is the determined cDNA sequence of clone
p0150r08c06

 SEQ ID NO:4511 is the determined cDNA sequence of clone
p0150r13c19

 SEQ ID NO:4512 is the determined cDNA sequence of clone
20 p0150r12c09

 SEQ ID NO:4513 is the determined cDNA sequence of clone
p0150r11c03

 SEQ ID NO:4514 is the determined cDNA sequence of clone
p0150r12c08

25 SEQ ID NO:4515 is the determined cDNA sequence of clone
p0150r05c22

 SEQ ID NO:4516 is the determined cDNA sequence of clone
p0150r09c11

 SEQ ID NO:4517 is the determined cDNA sequence of clone
30 p0150r15c23

SEQ ID NO:4518 is the determined cDNA sequence of clone
p0157r05c17

SEQ ID NO:4519 is the determined cDNA sequence of clone
p0157r07c13

5 SEQ ID NO:4520 is the determined cDNA sequence of clone
p0157r07c14

 SEQ ID NO:4521 is the determined cDNA sequence of clone
p0157r07c15

 SEQ ID NO:4522 is the determined cDNA sequence of clone
10 p0151r01c08

 SEQ ID NO:4523 is the determined cDNA sequence of clone
p0155r07c16

 SEQ ID NO:4524 is the determined cDNA sequence of clone
p0152r06c10

15 SEQ ID NO:4525 is the determined cDNA sequence of clone
p0150r04c18

 SEQ ID NO:4526 is the determined cDNA sequence of clone
p0150r02c03

 SEQ ID NO:4527 is the determined cDNA sequence of clone
20 p0150r06c24

 SEQ ID NO:4528 is the determined cDNA sequence of clone
p0150r11c14

 SEQ ID NO:4529 is the determined cDNA sequence of clone
p0157r05c18

25 SEQ ID NO:4530 is the determined cDNA sequence of clone
p0157r06c17

 SEQ ID NO:4531 is the determined cDNA sequence of clone
p0157r07c18

 SEQ ID NO:4532 is the determined cDNA sequence of clone
30 p0157r06c08

SEQ ID NO:4533 is the determined cDNA sequence of clone
p0157r07c23

SEQ ID NO:4534 is the determined cDNA sequence of clone
p0150r01c20

5 SEQ ID NO:4535 is the determined cDNA sequence of clone
p0150r14c15

 SEQ ID NO:4536 is the determined cDNA sequence of clone
p0150r15c06

 SEQ ID NO:4537 is the determined cDNA sequence of clone
10 p0151r12c17

 SEQ ID NO:4538 is the determined cDNA sequence of clone
p0155r12c15

 SEQ ID NO:4539 is the determined cDNA sequence of clone
p0157r07c09

15 SEQ ID NO:4540 is the determined cDNA sequence of clone
p0157r08c05

 SEQ ID NO:4541 is the determined cDNA sequence of clone
p0157r08c17

 SEQ ID NO:4542 is the determined cDNA sequence of clone
20 p0160r03c01

 SEQ ID NO:4543 is the determined cDNA sequence of clone
p0161r16c06

 SEQ ID NO:4544 is the determined cDNA sequence of clone
p0162r02c05

25 SEQ ID NO:4545 is the determined cDNA sequence of clone
p0157r06c24

 SEQ ID NO:4546 is the determined cDNA sequence of clone
p0157r07c06

 SEQ ID NO:4547 is the determined full length cDNA sequence of
30 Pn1467P

SEQ ID NO:4548 is the determined full length cDNA sequence of
10 Pn1468P.

SEQ ID NO:4549 is the determined full length cDNA sequence of
15 Pn1472P.

5 SEQ ID NO:4550 is the determined full length cDNA sequence of
Pn1475P.

SEQ ID NO:4551 is the full length protein sequence of Pn1467P.

SEQ ID NO:4552 is the full length protein sequence of Pn1468P.

SEQ ID NO:4553 is the full length protein sequence of Pn1472P.

10 SEQ ID NO:4554 is the full length protein sequence of Pn1475P.

SEQ ID NO:4555 is the full length cDNA sequence of Pn1509P.

SEQ ID NO:4556 is the full length cDNA sequence of Pn1510P-short,
encoding a 243 amino acid ORF of Pn1510P as set forth in SEQ ID NO:4559.

15 SEQ ID NO:4557 is the full length cDNA sequence of Pn1510P-long,
encoding a 278 amino acid ORF of Pn1510P as set forth in SEQ ID NO:4560.

SEQ ID NO:4558 is the full length protein sequence of Pn1509P,
encoded by the cDNA set forth in SEQ ID NO:4555.

SEQ ID NO:4559 is the amino acid sequence of the Pn1510P-243 ORF
encoded by the cDNA sequence set forth in SEQ ID NO:4556.

20 SEQ ID NO:4560 is the amino acid sequence of the Pn1510P-278 ORF
encoded by the cDNA sequence set forth in SEQ ID NO:4557.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed generally to compositions and their use
in the therapy and diagnosis of cancer, particularly pancreatic cancer. As described
25 further below, illustrative compositions of the present invention include, but are not
restricted to, polypeptides, particularly immunogenic polypeptides, polynucleotides
encoding such polypeptides, antibodies and other binding agents, antigen presenting
cells (APCs) and immune system cells (*e.g.*, T cells).

The practice of the present invention will employ, unless indicated
30 specifically to the contrary, conventional methods of virology, immunology,

microbiology, molecular biology and recombinant DNA techniques within the skill of the art, many of which are described below for the purpose of illustration. Such techniques are explained fully in the literature. See, e.g., Sambrook, et al. Molecular Cloning: A Laboratory Manual (2nd Edition, 1989); Maniatis et al. Molecular Cloning:

- 5 A Laboratory Manual (1982); DNA Cloning: A Practical Approach, vol. I & II (D. Glover, ed.); Oligonucleotide Synthesis (N. Gait, ed., 1984); Nucleic Acid Hybridization (B. Hames & S. Higgins, eds., 1985); Transcription and Translation (B. Hames & S. Higgins, eds., 1984); Animal Cell Culture (R. Freshney, ed., 1986); Perbal, A Practical Guide to Molecular Cloning (1984).

- 10 All publications, patents and patent applications cited herein, whether supra or infra, are hereby incorporated by reference in their entirety.

As used in this specification and the appended claims, the singular forms "a," "an" and "the" include plural references unless the content clearly dictates otherwise.

15 Polypeptide Compositions

As used herein, the term "polypeptide" is used in its conventional meaning, i.e., as a sequence of amino acids. The polypeptides are not limited to a specific length of the product; thus, peptides, oligopeptides, and proteins are included within the definition of polypeptide, and such terms may be used interchangeably herein unless specifically indicated otherwise. This term also does not refer to or exclude post-expression modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like, as well as other modifications known in the art, both naturally occurring and non-naturally occurring. A polypeptide may be an entire protein, or a subsequence thereof. Particular polypeptides of interest in the context of this invention are amino acid subsequences comprising epitopes, i.e., antigenic determinants substantially responsible for the immunogenic properties of a polypeptide and being capable of evoking an immune response.

Particularly illustrative polypeptides of the present invention comprise those encoded by a polynucleotide sequence set forth in any one of SEQ ID NOs:1-66, 30 75-152, 174-177, 182, 184-452, and 454-4550, or a sequence that hybridizes under

moderately stringent conditions, or, alternatively, under highly stringent conditions, to a polynucleotide sequence set forth in any one of SEQ ID NOS:1-66, 75-152, 174-177, 182, 184-452, and 454-4550. Certain other illustrative polypeptides of the invention comprise amino acid sequences as set forth in any one of SEQ ID NOS:67-74, 153-173, 5 178-181, 183, 453, 4551-4554 and 4558-4560.

The polypeptides of the present invention are sometimes herein referred to as pancreatic tumor proteins or pancreatic tumor polypeptides, as an indication that their identification has been based at least in part upon their increased levels of expression in pancreatic tumor samples. Thus, a "pancreatic tumor polypeptide" or 10 "pancreatic tumor protein," refers generally to a polypeptide sequence of the present invention, or a polynucleotide sequence encoding such a polypeptide, that is expressed in a substantial proportion of pancreatic tumor samples, for example preferably greater than about 20%, more preferably greater than about 30%, and most preferably greater than about 50% or more of pancreatic tumor samples tested, at a level that is at least 15 two fold, and preferably at least five fold, greater than the level of expression in normal tissues, as determined using a representative assay provided herein. A pancreatic tumor polypeptide sequence of the invention, based upon its increased level of expression in tumor cells, has particular utility both as a diagnostic marker as well as a therapeutic target, as further described below.

In certain preferred embodiments, the polypeptides of the invention are 20 immunogenic, *i.e.*, they react detectably within an immunoassay (such as an ELISA or T-cell stimulation assay) with antisera and/or T-cells from a patient with pancreatic cancer. Screening for immunogenic activity can be performed using techniques well known to the skilled artisan. For example, such screens can be performed using 25 methods such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In one illustrative example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I- 30 labeled Protein A.

As would be recognized by the skilled artisan, immunogenic portions of the polypeptides disclosed herein are also encompassed by the present invention. An "immunogenic portion," as used herein, is a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive (*i.e.*, specifically binds) with the 5 B-cells and/or T-cell surface antigen receptors that recognize the polypeptide. Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or 10 clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well-known techniques.

In one preferred embodiment, an immunogenic portion of a polypeptide 15 of the present invention is a portion that reacts with antisera and/or T-cells at a level that is not substantially less than the reactivity of the full-length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Preferably, the level of immunogenic activity of the immunogenic portion is at least about 50%, preferably at least about 70% and most preferably greater than about 90% of the immunogenicity for the full-length 20 polypeptide. In some instances, preferred immunogenic portions will be identified that have a level of immunogenic activity greater than that of the corresponding full-length polypeptide, *e.g.*, having greater than about 100% or 150% or more immunogenic activity.

In certain other embodiments, illustrative immunogenic portions may 25 include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other illustrative immunogenic portions will contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

In another embodiment, a polypeptide composition of the invention may 30 also comprise one or more polypeptides that are immunologically reactive with T cells and/or antibodies generated against a polypeptide of the invention, particularly a

polypeptide having an amino acid sequence disclosed herein, or to an immunogenic fragment or variant thereof.

In another embodiment of the invention, polypeptides are provided that comprise one or more polypeptides that are capable of eliciting T cells and/or antibodies 5 that are immunologically reactive with one or more polypeptides described herein, or one or more polypeptides encoded by contiguous nucleic acid sequences contained in the polynucleotide sequences disclosed herein, or immunogenic fragments or variants thereof, or to one or more nucleic acid sequences which hybridize to one or more of these sequences under conditions of moderate to high stringency.

10 The present invention, in another aspect, provides polypeptide fragments comprising at least about 5, 10, 15, 20, 25, 50, or 100 contiguous amino acids, or more, including all intermediate lengths, of a polypeptide compositions set forth herein, such as those set forth in SEQ ID NOs:67-74, 153-173, 178-181, 183, 453, 4551-4554 and 4558-4560, or those encoded by a polynucleotide sequence set forth in a sequence of 15 SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550.

In another aspect, the present invention provides variants of the polypeptide compositions described herein. Polypeptide variants generally encompassed by the present invention will typically exhibit at least about 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% or more identity 20 (determined as described below), along its length, to a polypeptide sequences set forth herein.

In one preferred embodiment, the polypeptide fragments and variants provided by the present invention are immunologically reactive with an antibody and/or T-cell that reacts with a full-length polypeptide specifically set forth herein.

25 In another preferred embodiment, the polypeptide fragments and variants provided by the present invention exhibit a level of immunogenic activity of at least about 50%, preferably at least about 70%, and most preferably at least about 90% or more of that exhibited by a full-length polypeptide sequence specifically set forth herein.

30 A polypeptide "variant," as the term is used herein, is a polypeptide that typically differs from a polypeptide specifically disclosed herein in one or more

substitutions, deletions, additions and/or insertions. Such variants may be naturally occurring or may be synthetically generated, for example, by modifying one or more of the above polypeptide sequences of the invention and evaluating their immunogenic activity as described herein and/or using any of a number of techniques well known in
5 the art.

For example, certain illustrative variants of the polypeptides of the invention include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other illustrative variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino
10 acids) has been removed from the N- and/or C-terminal of the mature protein.

In many instances, a variant will contain conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydrophobic nature of the
15 polypeptide to be substantially unchanged. As described above, modifications may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional molecule that encodes a variant or derivative polypeptide with desirable characteristics, e.g., with immunogenic characteristics. When it is desired to alter the amino acid sequence of a polypeptide to create an equivalent, or
20 even an improved, immunogenic variant or portion of a polypeptide of the invention, one skilled in the art will typically change one or more of the codons of the encoding DNA sequence according to Table 1.

For example, certain amino acids may be substituted for other amino acids in a protein structure without appreciable loss of interactive binding capacity with
25 structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless obtain a protein with like properties. It is thus contemplated that various changes may be made in the peptide sequences of the
30

disclosed compositions, or corresponding DNA sequences which encode said peptides without appreciable loss of their biological utility or activity.

TABLE I

5

Amino Acids		Codons					
Alanine	Ala	A	GCA	GCC	GCG	GCU	
Cysteine	Cys	C	UGC	UGU			
Aspartic acid	Asp	D	GAC	GAU			
Glutamic acid	Glu	E	GAA	GAG			
Phenylalanine	Phe	F	UUC	UUU			
Glycine	Gly	G	GGA	GGC	GGG	GGU	
Histidine	His	H	CAC	CAU			
Isoleucine	Ile	I	AUA	AUC	AUU		
Lysine	Lys	K	AAA	AAG			
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG
Methionine	Met	M	AUG				
Asparagine	Asn	N	AAC	AAU			
Proline	Pro	P	CCA	CCC	CCG	CCU	
Glutamine	Gln	Q	CAA	CAG			
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG
Threonine	Thr	T	ACA	ACC	ACG	ACU	
Valine	Val	V	GUU	GUC	GUG	GUU	
Tryptophan	Trp	W	UGG				
Tyrosine	Tyr	Y	UAC	UAU			

In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference). It is accepted that the relative 10 hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and

the like. Each amino acid has been assigned a hydrophobic index on the basis of its hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (-0.4); threonine (-0.7); serine (-0.8); tryptophan (-0.9); tyrosine (-1.3); proline (-1.6); histidine (-3.2); glutamate (-3.5); glutamine (-3.5); aspartate (-3.5); asparagine (-3.5); lysine (-3.9); and arginine (-4.5).

It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydrophobic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose hydrophobic indices are within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U. S. Patent 4,554,101 (specifically incorporated herein by reference in its entirety), states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of its adjacent amino acids, correlates with a biological property of the protein.

As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate ($+3.0 \pm 1$); glutamate ($+3.0 \pm 1$); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (-0.4); proline (-0.5 ± 1); alanine (-0.5); histidine (-0.5); cysteine (-1.0); methionine (-1.3); valine (-1.5); leucine (-1.8); isoleucine (-1.8); tyrosine (-2.3); phenylalanine (-2.5); tryptophan (-3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In such changes, the substitution of amino acids whose hydrophilicity values are within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred.

As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their

hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that take various of the foregoing characteristics into consideration are well known to those of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

5 In addition, any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiester linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-
10 methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Amino acid substitutions may further be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic
15 acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr,
20 (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that
25 have minimal influence on the immunogenicity, secondary structure and hydrophatic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated
30 to a linker or other sequence for ease of synthesis, purification or identification of the

polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

When comparing polypeptide sequences, two sequences are said to be "identical" if the sequence of amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) *Unified Approach to Alignment and Phylogenies* pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and 25 Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) 30 *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics

Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 5 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for 10 Biotechnology Information. For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is 15 reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

In one preferred approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polypeptide sequence in 20 the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of 25 matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Within other illustrative embodiments, a polypeptide may be a xenogeneic polypeptide that comprises an polypeptide having substantial sequence 30 identity, as described above, to the human polypeptide (also termed autologous antigen) which served as a reference polypeptide, but which xenogeneic polypeptide is derived

from a different, non-human species. One skilled in the art will recognize that "self" antigens are often poor stimulators of CD8+ and CD4+ T-lymphocyte responses, and therefore efficient immunotherapeutic strategies directed against tumor polypeptides require the development of methods to overcome immune tolerance to 5 particular self tumor polypeptides. For example, humans immunized with prostase protein from a xenogeneic (non human) origin are capable of mounting an immune response against the counterpart human protein, e.g. the human prostase tumor protein present on human tumor cells. Accordingly, the present invention provides methods for purifying the xenogeneic form of the tumor proteins set forth herein, such as the 10 polypeptides set forth in SEQ ID NOs:67-74, 153-173, 178-181, 183, 453, 4551-4554 and 4558-4560, or those encoded by polynucleotide sequences set forth in SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452 and 454-4550.

Therefore, one aspect of the present invention provides xenogeneic variants of the polypeptide compositions described herein. Such xenogeneic variants 15 generally encompassed by the present invention will typically exhibit at least about 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% or more identity along their lengths, to a polypeptide sequences set forth herein.

More particularly, the invention is directed to mouse, rat, monkey, porcine and other non-human polypeptides which can be used as xenogeneic forms of 20 human polypeptides set forth herein, to induce immune responses directed against tumor polypeptides of the invention.

Within other illustrative embodiments, a polypeptide may be a fusion polypeptide that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known 25 tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be 30 selected so as to increase the solubility of the polypeptide or to enable the polypeptide

to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the polypeptide.

Fusion polypeptides may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion polypeptide is
5 expressed as a recombinant polypeptide, allowing the production of increased levels, relative to a non-fused polypeptide, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a
10 DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion polypeptide that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide
15 folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion polypeptide using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors:
(1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second
20 polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al.,
25 *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

30 The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements

responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

5 The fusion polypeptide can comprise a polypeptide as described herein together with an unrelated immunogenic protein, such as an immunogenic protein capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91, 1997).

10 In one preferred embodiment, the immunological fusion partner is derived from a *Mycobacterium* sp., such as a *Mycobacterium tuberculosis*-derived Ra12 fragment. Ra12 compositions and methods for their use in enhancing the expression and/or immunogenicity of heterologous polynucleotide/polypeptide sequences is described in U.S. Patent Application 60/158,585, the disclosure of which is 15 incorporated herein by reference in its entirety. Briefly, Ra12 refers to a polynucleotide region that is a subsequence of a *Mycobacterium tuberculosis* MTB32A nucleic acid. MTB32A is a serine protease of 32 KD molecular weight encoded by a gene in virulent and avirulent strains of *M. tuberculosis*. The nucleotide sequence and amino acid sequence of MTB32A have been described (for example, U.S. Patent Application 20 60/158,585; see also, Skeiky et al., *Infection and Immun.* (1999) 67:3998-4007, incorporated herein by reference). C-terminal fragments of the MTB32A coding sequence express at high levels and remain as a soluble polypeptides throughout the purification process. Moreover, Ra12 may enhance the immunogenicity of heterologous immunogenic polypeptides with which it is fused. One preferred Ra12 fusion 25 polypeptide comprises a 14 KD C-terminal fragment corresponding to amino acid residues 192 to 323 of MTB32A. Other preferred Ra12 polynucleotides generally comprise at least about 15 consecutive nucleotides, at least about 30 nucleotides, at least about 60 nucleotides, at least about 100 nucleotides, at least about 200 nucleotides, or at least about 300 nucleotides that encode a portion of a Ra12 polypeptide. Ra12 30 polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes a Ra12 polypeptide or a portion thereof) or may comprise a variant of such a

sequence. Ra12 polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not substantially diminished, relative to a fusion polypeptide comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70%
5 identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide or a portion thereof.

Within other preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to
15 increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.
16

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the LytA gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan
25 backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798, 30 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated

into a fusion polypeptide. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

Yet another illustrative embodiment involves fusion polypeptides, and the polynucleotides encoding them, wherein the fusion partner comprises a targeting signal capable of directing a polypeptide to the endosomal/lysosomal compartment, as described in U.S. Patent No. 5,633,234. An immunogenic polypeptide of the invention, when fused with this targeting signal, will associate more efficiently with MHC class II molecules and thereby provide enhanced *in vivo* stimulation of CD4⁺ T-cells specific for the polypeptide.

10 Polypeptides of the invention are prepared using any of a variety of well known synthetic and/or recombinant techniques, the latter of which are further described below. Polypeptides, portions and other variants generally less than about 150 amino acids can be generated by synthetic means, using techniques well known to those of ordinary skill in the art. In one illustrative example, such polypeptides are 15 synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. *See Merrifield, J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and 20 may be operated according to the manufacturer's instructions.

In general, polypeptide compositions (including fusion polypeptides) of the invention are isolated. An "isolated" polypeptide is one that is removed from its original environment. For example, a naturally-occurring protein or polypeptide is isolated if it is separated from some or all of the coexisting materials in the natural 25 system. Preferably, such polypeptides are also purified, e.g., are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure.

Polynucleotide Compositions

The present invention, in other aspects, provides polynucleotide 30 compositions. The terms "DNA" and "polynucleotide" are used essentially

interchangeably herein to refer to a DNA molecule that has been isolated free of total genomic DNA of a particular species. "Isolated," as used herein, means that a polynucleotide is substantially away from other coding sequences, and that the DNA molecule does not contain large portions of unrelated coding DNA, such as large 5 chromosomal fragments or other functional genes or polypeptide coding regions. Of course, this refers to the DNA molecule as originally isolated, and does not exclude genes or coding regions later added to the segment by the hand of man.

As will be understood by those skilled in the art, the polynucleotide compositions of this invention can include genomic sequences, extra-genomic and 10 plasmid-encoded sequences and smaller engineered gene segments that express, or may be adapted to express, proteins, polypeptides, peptides and the like. Such segments may be naturally isolated, or modified synthetically by the hand of man.

As will be also recognized by the skilled artisan, polynucleotides of the invention may be single-stranded (coding or antisense) or double-stranded, and may be 15 DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules may include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules 20 and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a polypeptide/protein of the invention or a portion thereof) or may comprise a sequence that encodes a variant or derivative, preferably and immunogenic variant or derivative, of such a sequence.

25 Therefore, according to another aspect of the present invention, polynucleotide compositions are provided that comprise some or all of a polynucleotide sequence set forth in any one of SEQ ID NOS:1-66, 75-152, 174-177, 182, 184-452, and 454-4550, complements of a polynucleotide sequence set forth in any one of SEQ ID NOS:1-66, 75-152, 174-177, 182, 184-452, and 454-4550, and degenerate variants of a 30 polynucleotide sequence set forth in any one of SEQ ID NOS:1-66, 75-152, 174-177,

182, 184-452, and 454-4550. In certain preferred embodiments, the polynucleotide sequences set forth herein encode immunogenic polypeptides, as described above.

In other related embodiments, the present invention provides polynucleotide variants having substantial identity to the sequences disclosed herein in 5 SEQ ID NOS:1-66, 75-152, 174-177, 182, 184-452, and 454-4550, for example those comprising at least 70% sequence identity, preferably at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a polynucleotide sequence of this invention using the methods described herein, (e.g., BLAST analysis using standard parameters, as described below). One skilled in this art 10 will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning and the like.

Typically, polynucleotide variants will contain one or more substitutions, 15 additions, deletions and/or insertions, preferably such that the immunogenicity of the polypeptide encoded by the variant polynucleotide is not substantially diminished relative to a polypeptide encoded by a polynucleotide sequence specifically set forth herein). The term "variants" should also be understood to encompass homologous genes of xenogenic origin.

20 In additional embodiments, the present invention provides polynucleotide fragments comprising various lengths of contiguous stretches of sequence identical to or complementary to one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at least about 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more 25 contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. It will be readily understood that "intermediate lengths", in this context, means any length between the quoted values, such as 16, 17, 18, 19, etc.; 21, 22, 23, etc.; 30, 31, 32, etc.; 50, 51, 52, 53, etc.; 100, 101, 102, 103, etc.; 150, 151, 152, 153, etc.; including all integers through 200-500; 500-1,000, and the 30 like. A polynucleotide sequence as described here may be extended at one or both ends by additional nucleotides

not found in the native sequence. This additional sequence may consist of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 nucleotides at either end of the disclosed sequence or at both ends of the disclosed sequence.

In another embodiment of the invention, polynucleotide compositions 5 are provided that are capable of hybridizing under moderate to high stringency conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary sequence thereof. Hybridization techniques are well known in the art of molecular biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other 10 polynucleotides include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-60°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. One skilled in the art will understand that the stringency of hybridization can be readily manipulated, such as by altering the salt content of the hybridization solution 15 and/or the temperature at which the hybridization is performed. For example, in another embodiment, suitable highly stringent hybridization conditions include those described above, with the exception that the temperature of hybridization is increased, e.g., to 60-65°C or 65-70°C.

In certain preferred embodiments, the polynucleotides described above, 20 e.g., polynucleotide variants, fragments and hybridizing sequences, encode polypeptides that are immunologically cross-reactive with a polypeptide sequence specifically set forth herein. In other preferred embodiments, such polynucleotides encode polypeptides that have a level of immunogenic activity of at least about 50%, preferably at least about 70%, and more preferably at least about 90% of that for a 25 polypeptide sequence specifically set forth herein.

The polynucleotides of the present invention, or fragments thereof, regardless of the length of the coding sequence itself, may be combined with other DNA sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their 30 overall length may vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being

limited by the ease of preparation and use in the intended recombinant DNA protocol. For example, illustrative polynucleotide segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like, (including all intermediate lengths) are
5 contemplated to be useful in many implementations of this invention.

When comparing polynucleotide sequences, two sequences are said to be "identical" if the sequence of nucleotides in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison
10 window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

15 Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships.
20 In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson,
25 E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

30 Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J.*

Mol. Biol. 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI),

5 or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST

10 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; 15 always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T and X 20 determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

25 Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does 30 not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical

nucleic acid bases occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

5 It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present
10 invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard
15 techniques (such as hybridization, amplification and/or database sequence comparison).

Therefore, in another embodiment of the invention, a mutagenesis approach, such as site-specific mutagenesis, is employed for the preparation of immunogenic variants and/or derivatives of the polypeptides described herein. By this approach, specific modifications in a polypeptide sequence can be made through
20 mutagenesis of the underlying polynucleotides that encode them. These techniques provides a straightforward approach to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more nucleotide sequence changes into the polynucleotide.

Site-specific mutagenesis allows the production of mutants through the
25 use of specific oligonucleotide sequences which encode the DNA sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on both sides of the deletion junction being traversed. Mutations may be employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise
30 change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

In certain embodiments of the present invention, the inventors contemplate the mutagenesis of the disclosed polynucleotide sequences to alter one or more properties of the encoded polypeptide, such as the immunogenicity of a polypeptide vaccine. The techniques of site-specific mutagenesis are well-known in the art, and are widely used to create variants of both polypeptides and polynucleotides. For example, site-specific mutagenesis is often used to alter a specific portion of a DNA molecule. In such embodiments, a primer comprising typically about 14 to about 25 nucleotides or so in length is employed, with about 5 to about 10 residues on both sides of the junction of the sequence being altered.

- 10 As will be appreciated by those of skill in the art, site-specific mutagenesis techniques have often employed a phage vector that exists in both a single stranded and double stranded form. Typical vectors useful in site-directed mutagenesis include vectors such as the M13 phage. These phage are readily commercially-available and their use is generally well-known to those skilled in the art.
- 15 Double-stranded plasmids are also routinely employed in site directed mutagenesis that eliminates the step of transferring the gene of interest from a plasmid to a phage.

In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a double-stranded vector that includes within its sequence a DNA sequence that encodes 20 the desired peptide. An oligonucleotide primer bearing the desired mutated sequence is prepared, generally synthetically. This primer is then annealed with the single-stranded vector, and subjected to DNA polymerizing enzymes such as *E. coli* polymerase I Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated 25 sequence and the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells, such as *E. coli* cells, and clones are selected which include recombinant vectors bearing the mutated sequence arrangement.

The preparation of sequence variants of the selected peptide-encoding DNA segments using site-directed mutagenesis provides a means of producing 30 potentially useful species and is not meant to be limiting as there are other ways in which sequence variants of peptides and the DNA sequences encoding them may be

obtained. For example, recombinant vectors encoding the desired peptide sequence may be treated with mutagenic agents, such as hydroxylamine, to obtain sequence variants. Specific details regarding these methods and protocols are found in the teachings of Maloy *et al.*, 1994; Segal, 1976; Prokop and Bajpai, 1991; Kuby, 1994; 5 and Maniatis *et al.*, 1982, each incorporated herein by reference, for that purpose.

As used herein, the term "oligonucleotide directed mutagenesis procedure" refers to template-dependent processes and vector-mediated propagation which result in an increase in the concentration of a specific nucleic acid molecule relative to its initial concentration, or in an increase in the concentration of a detectable 10 signal, such as amplification. As used herein, the term "oligonucleotide directed mutagenesis procedure" is intended to refer to a process that involves the template-dependent extension of a primer molecule. The term template dependent process refers to nucleic acid synthesis of an RNA or a DNA molecule wherein the sequence of the newly synthesized strand of nucleic acid is dictated by the well-known 15 rules of complementary base pairing (see, for example, Watson, 1987). Typically, vector mediated methodologies involve the introduction of the nucleic acid fragment into a DNA or RNA vector, the clonal amplification of the vector, and the recovery of the amplified nucleic acid fragment. Examples of such methodologies are provided by U. S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety.

20 In another approach for the production of polypeptide variants of the present invention, recursive sequence recombination, as described in U.S. Patent No. 5,837,458, may be employed. In this approach, iterative cycles of recombination and screening or selection are performed to "evolve" individual polynucleotide variants of the invention having, for example, enhanced immunogenic activity.

25 In other embodiments of the present invention, the polynucleotide sequences provided herein can be advantageously used as probes or primers for nucleic acid hybridization. As such, it is contemplated that nucleic acid segments that comprise a sequence region of at least about 15 nucleotide long contiguous sequence that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence 30 disclosed herein will find particular utility. Longer contiguous identical or complementary sequences, e.g., those of about 20, 30, 40, 50, 100, 200, 500, 1000

(including all intermediate lengths) and even up to full length sequences will also be of use in certain embodiments.

The ability of such nucleic acid probes to specifically hybridize to a sequence of interest will enable them to be of use in detecting the presence of 5 complementary sequences in a given sample. However, other uses are also envisioned, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions.

Polynucleotide molecules having sequence regions consisting of contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides 10 or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, e.g., Southern and Northern blotting. This would allow a gene product, or fragment thereof, to be analyzed, both in diverse cell types and also in various bacterial cells. The total size of fragment, as well as the size of the 15 complementary stretch(es), will ultimately depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the contiguous complementary region may be varied, such as between about 15 and about 100 nucleotides, but larger contiguous complementarity stretches may be used, according to the length 20 complementary sequences one wishes to detect.

The use of a hybridization probe of about 15-25 nucleotides in length allows the formation of a duplex molecule that is both stable and selective. Molecules having contiguous complementary sequences over stretches greater than 15 bases in length are generally preferred, though, in order to increase stability and selectivity of 25 the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. One will generally prefer to design nucleic acid molecules having gene-complementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired.

Hybridization probes may be selected from any portion of any of the 30 sequences disclosed herein. All that is required is to review the sequences set forth herein, or to any continuous portion of the sequences, from about 15-25 nucleotides in

length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences may be governed by various factors. For example, one may wish to employ primers from towards the termini of the total sequence.

5 Small polynucleotide segments or fragments may be readily prepared by, for example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments may be obtained by application of nucleic acid reproduction technology, such as the PCR™ technology of U. S. Patent 4,683,202 (incorporated herein by reference), by introducing
10 selected sequences into recombinant vectors for recombinant production, and by other recombinant DNA techniques generally known to those of skill in the art of molecular biology.

The nucleotide sequences of the invention may be used for their ability to selectively form duplex molecules with complementary stretches of the entire gene or
15 gene fragments of interest. Depending on the application envisioned, one will typically desire to employ varying conditions of hybridization to achieve varying degrees of selectivity of probe towards target sequence. For applications requiring high selectivity, one will typically desire to employ relatively stringent conditions to form the hybrids, e.g., one will select relatively low salt and/or high temperature conditions, such as
20 provided by a salt concentration of from about 0.02 M to about 0.15 M salt at temperatures of from about 50°C to about 70°C. Such selective conditions tolerate little, if any, mismatch between the probe and the template or target strand, and would be particularly suitable for isolating related sequences.

Of course, for some applications, for example, where one desires to
25 prepare mutants employing a mutant primer strand hybridized to an underlying template, less stringent (reduced stringency) hybridization conditions will typically be needed in order to allow formation of the heteroduplex. In these circumstances, one may desire to employ salt conditions such as those of from about 0.15 M to about 0.9 M salt, at temperatures ranging from about 20°C to about 55°C. Cross-hybridizing species
30 can thereby be readily identified as positively hybridizing signals with respect to control hybridizations. In any case, it is generally appreciated that conditions can be rendered

more stringent by the addition of increasing amounts of formamide, which serves to destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions can be readily manipulated, and thus will generally be a method of choice depending on the desired results.

- 5 According to another embodiment of the present invention, polynucleotide compositions comprising antisense oligonucleotides are provided. Antisense oligonucleotides have been demonstrated to be effective and targeted inhibitors of protein synthesis, and, consequently, provide a therapeutic approach by which a disease can be treated by inhibiting the synthesis of proteins that contribute to
10 the disease. The efficacy of antisense oligonucleotides for inhibiting protein synthesis is well established. For example, the synthesis of polygalacturonase and the muscarine type 2 acetylcholine receptor are inhibited by antisense oligonucleotides directed to their respective mRNA sequences (U. S. Patent 5,739,119 and U. S. Patent 5,759,829). Further, examples of antisense inhibition have been demonstrated with the nuclear
15 protein cyclin, the multiple drug resistance gene (MDG1), ICAM-1, E-selectin, STK-1, striatal GABA_A receptor and human EGF (Jaskulski *et al.*, Science. 1988 Jun 10;240(4858):1544-6; VasanthaKumar and Ahmed, Cancer Commun. 1989;1(4):225-32; Peris *et al.*, Brain Res Mol Brain Res. 1998 Jun 15;57(2):310-20; U. S. Patent 5,801,154; U.S. Patent 5,789,573; U. S. Patent 5,718,709 and U.S. Patent 5,610,288).
20 Antisense constructs have also been described that inhibit and can be used to treat a variety of abnormal cellular proliferations, e.g. cancer (U. S. Patent 5,747,470; U. S. Patent 5,591,317 and U. S. Patent 5,783,683).

Therefore, in certain embodiments, the present invention provides
25 oligonucleotide sequences that comprise all, or a portion of, any sequence that is capable of specifically binding to polynucleotide sequence described herein, or a complement thereof. In one embodiment, the antisense oligonucleotides comprise DNA or derivatives thereof. In another embodiment, the oligonucleotides comprise RNA or derivatives thereof. In a third embodiment, the oligonucleotides are modified DNAs comprising a phosphorothioated modified backbone. In a fourth embodiment, the
30 oligonucleotide sequences comprise peptide nucleic acids or derivatives thereof. In each case, preferred compositions comprise a sequence region that is complementary,

and more preferably substantially-complementary, and even more preferably, completely complementary to one or more portions of polynucleotides disclosed herein. Selection of antisense compositions specific for a given gene sequence is based upon analysis of the chosen target sequence and determination of secondary structure, T_m ,
5 binding energy, and relative stability. Antisense compositions may be selected based upon their relative inability to form dimers, hairpins, or other secondary structures that would reduce or prohibit specific binding to the target mRNA in a host cell. Highly preferred target regions of the mRNA, are those which are at or near the AUG translation initiation codon, and those sequences which are substantially complementary
10 to 5' regions of the mRNA. These secondary structure analyses and target site selection considerations can be performed, for example, using v.4 of the OLIGO primer analysis software and/or the BLASTN 2.0.5 algorithm software (Altschul *et al.*, Nucleic Acids Res. 1997, 25(17):3389-402).

The use of an antisense delivery method employing a short peptide
15 vector, termed MPG (27 residues), is also contemplated. The MPG peptide contains a hydrophobic domain derived from the fusion sequence of HIV gp41 and a hydrophilic domain from the nuclear localization sequence of SV40 T-antigen (Morris *et al.*, Nucleic Acids Res. 1997 Jul 15;25(14):2730-6). It has been demonstrated that several molecules of the MPG peptide coat the antisense oligonucleotides and can be delivered
20 into cultured mammalian cells in less than 1 hour with relatively high efficiency (90%). Further, the interaction with MPG strongly increases both the stability of the oligonucleotide to nuclease and the ability to cross the plasma membrane.

According to another embodiment of the invention, the polynucleotide compositions described herein are used in the design and preparation of ribozyme
25 molecules for inhibiting expression of the tumor polypeptides and proteins of the present invention in tumor cells. Ribozymes are RNA-protein complexes that cleave nucleic acids in a site-specific fashion. Ribozymes have specific catalytic domains that possess endonuclease activity (Kim and Cech, Proc Natl Acad Sci U S A. 1987 Dec;84(24):8788-92; Forster and Symons, Cell. 1987 Apr 24;49(2):211-20). For
30 example, a large number of ribozymes accelerate phosphoester transfer reactions with a high degree of specificity, often cleaving only one of several phosphoesters in an

oligonucleotide substrate (Cech *et al.*, Cell. 1981 Dec;27(3 Pt 2):487-96; Michel and Westhof, J Mol Biol. 1990 Dec 5;216(3):585-610; Reinhold-Hurek and Shub, Nature. 1992 May 14;357(6374):173-6). This specificity has been attributed to the requirement that the substrate bind via specific base-pairing interactions to the internal guide sequence ("IGS") of the ribozyme prior to chemical reaction.

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds *in trans* (and thus can cleave other RNA molecules) under physiological conditions. In general, enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets.

The enzymatic nature of a ribozyme is advantageous over many technologies, such as antisense technology (where a nucleic acid molecule simply binds to a nucleic acid target to block its translation) since the concentration of ribozyme necessary to affect a therapeutic treatment is lower than that of an antisense oligonucleotide. This advantage reflects the ability of the ribozyme to act enzymatically. Thus, a single ribozyme molecule is able to cleave many molecules of target RNA. In addition, the ribozyme is a highly specific inhibitor, with the specificity of inhibition depending not only on the base pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme. Similar mismatches in antisense molecules do not prevent their action (Woolf *et al.*, Proc Natl Acad Sci U S A. 1992 Aug 15;89(16):7305-9). Thus, the specificity of action of a ribozyme is greater than that of an antisense oligonucleotide binding the same RNA site.

The enzymatic nucleic acid molecule may be formed in a hammerhead, hairpin, a hepatitis 8 virus, group I intron or RNaseP RNA (in association with an RNA guide sequence) or Neurospora VS RNA motif. Examples of hammerhead motifs are described by Rossi *et al.* Nucleic Acids Res. 1992 Sep 11;20(17):4559-65. Examples of 5 hairpin motifs are described by Hampel *et al.* (Eur. Pat. Appl. Publ. No. EP 0360257), Hampel and Tritz, Biochemistry 1989 Jun 13;28(12):4929-33; Hampel *et al.*, Nucleic Acids Res. 1990 Jan 25;18(2):299-304 and U. S. Patent 5,631,359. An example of the hepatitis 8 virus motif is described by Perrotta and Been, Biochemistry. 1992 Dec 13;31(47):11843-52; an example of the RNaseP motif is described by Guerrier-Takada 10 *et al.*, Cell. 1983 Dec;35(3 Pt 2):849-57; Neurospora VS RNA ribozyme motif is described by Collins (Saville and Collins, Cell. 1990 May 18;61(4):685-96; Saville and Collins, Proc Natl Acad Sci U S A. 1991 Oct 1;88(19):8826-30; Collins and Olive, Biochemistry. 1993 Mar 23;32(11):2795-9); and an example of the Group I intron is described in (U. S. Patent 4,987,071). All that is important in an enzymatic nucleic acid 15 molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an RNA cleaving activity to the molecule. Thus the ribozyme constructs need not be limited to specific motifs mentioned herein.

20 Ribozymes may be designed as described in Int. Pat. Appl. Publ. No. WO 93/23569 and Int. Pat. Appl. Publ. No. WO 94/02595, each specifically incorporated herein by reference) and synthesized to be tested *in vitro* and *in vivo*, as described. Such ribozymes can also be optimized for delivery. While specific examples are provided, those in the art will recognize that equivalent RNA targets in 25 other species can be utilized when necessary.

Ribozyme activity can be optimized by altering the length of the ribozyme binding arms, or chemically synthesizing ribozymes with modifications that prevent their degradation by serum ribonucleases (see e.g., Int. Pat. Appl. Publ. No. WO 92/07065; Int. Pat. Appl. Publ. No. WO 93/15187; Int. Pat. Appl. Publ. No. WO 30 91/03162; Eur. Pat. Appl. Publ. No. 92110298.4; U. S. Patent 5,334,711; and Int. Pat. Appl. Publ. No. WO 94/13688, which describe various chemical modifications that can

be made to the sugar moieties of enzymatic RNA molecules), modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements.

Sullivan *et al.* (Int. Pat. Appl. Publ. No. WO 94/02595) describes the general methods for delivery of enzymatic RNA molecules. Ribozymes may be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be directly delivered *ex vivo* to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination may be locally delivered by direct inhalation, by direct injection or by use of a catheter, infusion pump or stent. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Int. Pat. Appl. Publ. No. WO 94/02595 and Int. Pat. Appl. Publ. No. WO 93/23569, each specifically incorporated herein by reference.

Another means of accumulating high concentrations of a ribozyme(s) within cells is to incorporate the ribozyme-encoding sequences into a DNA expression vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, *etc.*) present nearby. Prokaryotic RNA polymerase promoters may also be used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells. Ribozymes expressed from such promoters have been shown to function in mammalian cells. Such transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA

vectors (such as adenovirus or adeno-associated vectors), or viral RNA vectors (such as retroviral, semliki forest virus, sindbis virus vectors).

In another embodiment of the invention, peptide nucleic acids (PNAs) compositions are provided. PNA is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone (Good and Nielsen, *Antisense Nucleic Acid Drug Dev.* 1997 7(4) 431-37). PNA is able to be utilized in a number methods that traditionally have used RNA or DNA. Often PNA sequences perform better in techniques than the corresponding RNA or DNA sequences and have utilities that are not inherent to RNA or DNA. A review of PNA including methods of making, characteristics of, and methods of using, is provided by Corey (*Trends Biotechnol* 1997 Jun;15(6):224-9). As such, in certain embodiments, one may prepare PNA sequences that are complementary to one or more portions of the ACE mRNA sequence, and such PNA compositions may be used to regulate, alter, decrease, or reduce the translation of ACE-specific mRNA, and thereby alter the level of ACE activity in a host cell to which such PNA compositions have been administered.

PNAs have 2-aminoethyl-glycine linkages replacing the normal phosphodiester backbone of DNA (Nielsen *et al.*, *Science* 1991 Dec 6;254(5037):1497-500; Hanvey *et al.*, *Science*. 1992 Nov 27;258(5087):1481-5; Hyrup and Nielsen, *Bioorg Med Chem.* 1996 Jan;4(1):5-23). This chemistry has three important consequences: firstly, in contrast to DNA or phosphorothioate oligonucleotides, PNAs are neutral molecules; secondly, PNAs are achiral, which avoids the need to develop a stereoselective synthesis; and thirdly, PNA synthesis uses standard Boc or Fmoc protocols for solid-phase peptide synthesis, although other methods, including a modified Merrifield method, have been used.

PNA monomers or ready-made oligomers are commercially available from PerSeptive Biosystems (Framingham, MA). PNA syntheses by either Boc or Fmoc protocols are straightforward using manual or automated protocols (Norton *et al.*, *Bioorg Med Chem.* 1995 Apr;3(4):437-45). The manual protocol lends itself to the production of chemically modified PNAs or the simultaneous synthesis of families of closely related PNAs.

As with peptide synthesis, the success of a particular PNA synthesis will depend on the properties of the chosen sequence. For example, while in theory PNAs can incorporate any combination of nucleotide bases, the presence of adjacent purines can lead to deletions of one or more residues in the product. In expectation of this difficulty, it is suggested that, in producing PNAs with adjacent purines, one should repeat the coupling of residues likely to be added inefficiently. This should be followed by the purification of PNAs by reverse-phase high-pressure liquid chromatography, providing yields and purity of product similar to those observed during the synthesis of peptides.

- 10 Modifications of PNAs for a given application may be accomplished by coupling amino acids during solid-phase synthesis or by attaching compounds that contain a carboxylic acid group to the exposed N-terminal amine. Alternatively, PNAs can be modified after synthesis by coupling to an introduced lysine or cysteine. The ease with which PNAs can be modified facilitates optimization for better solubility or 15 for specific functional requirements. Once synthesized, the identity of PNAs and their derivatives can be confirmed by mass spectrometry. Several studies have made and utilized modifications of PNAs (for example, Norton *et al.*, Bioorg Med Chem. 1995 Apr;3(4):437-45; Petersen *et al.*, J Pept Sci. 1995 May-Jun;1(3):175-83; Orum *et al.*, Biotechniques. 1995 Sep;19(3):472-80; Footer *et al.*, Biochemistry. 1996 Aug 20;35(33):10673-9; Griffith *et al.*, Nucleic Acids Res. 1995 Aug 11;23(15):3003-8; Pardridge *et al.*, Proc Natl Acad Sci U S A. 1995 Jun 6;92(12):5592-6; Boffa *et al.*, Proc Natl Acad Sci U S A. 1995 Mar 14;92(6):1901-5; Gambacorti-Passerini *et al.*, Blood. 1996 Aug 15;88(4):1411-7; Armitage *et al.*, Proc Natl Acad Sci U S A. 1997 Nov 11;94(23):12320-5; Seeger *et al.*, Biotechniques. 1997 Sep;23(3):512-7). U.S. Patent 25 No. 5,700,922 discusses PNA-DNA-PNA chimeric molecules and their uses in diagnostics, modulating protein in organisms, and treatment of conditions susceptible to therapeutics.

- Methods of characterizing the antisense binding properties of PNAs are discussed in Rose (Anal Chem. 1993 Dec 15;65(24):3545-9) and Jensen *et al.* 30 (Biochemistry. 1997 Apr 22;36(16):5072-7). Rose uses capillary gel electrophoresis to determine binding of PNAs to their complementary oligonucleotide, measuring the

relative binding kinetics and stoichiometry. Similar types of measurements were made by Jensen *et al.* using BIACore™ technology.

Other applications of PNAs that have been described and will be apparent to the skilled artisan include use in DNA strand invasion, antisense inhibition, 5 mutational analysis, enhancers of transcription, nucleic acid purification, isolation of transcriptionally active genes, blocking of transcription factor binding, genome cleavage, biosensors, *in situ* hybridization, and the like.

Polynucleotide Identification, Characterization and Expression

Polynucleotides compositions of the present invention may be identified, 10 prepared and/or manipulated using any of a variety of well established techniques (see generally, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989, and other like references). For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that 15 is at least two fold greater in a tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed, for example, using the microarray technology of Affymetrix, Inc. (Santa Clara, CA) according to the manufacturer's instructions (and essentially as described by Schena *et al.*, *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller *et al.*, *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polynucleotides may be amplified from cDNA 20 prepared from cells expressing the proteins described herein, such as tumor cells.

Many template dependent processes are available to amplify a target sequences of interest present in a sample. One of the best known amplification methods is the polymerase chain reaction (PCR™) which is described in detail in U.S. Patent 25 Nos. 4,683,195, 4,683,202 and 4,800,159, each of which is incorporated herein by reference in its entirety. Briefly, in PCR™, two primer sequences are prepared which are complementary to regions on opposite complementary strands of the target sequence. An excess of deoxynucleoside triphosphates is added to a reaction mixture along with a DNA polymerase (*e.g.*, *Taq* polymerase). If the target sequence is present 30 in a sample, the primers will bind to the target and the polymerase will cause the

primers to be extended along the target sequence by adding on nucleotides. By raising and lowering the temperature of the reaction mixture, the extended primers will dissociate from the target to form reaction products, excess primers will bind to the target and to the reaction product and the process is repeated. Preferably reverse transcription and PCR™ amplification procedure may be performed in order to quantify the amount of mRNA amplified. Polymerase chain reaction methodologies are well known in the art.

Any of a number of other template dependent processes, many of which are variations of the PCR™ amplification technique, are readily known and available in the art. Illustratively, some such methods include the ligase chain reaction (referred to as LCR), described, for example, in Eur. Pat. Appl. Publ. No. 320,308 and U.S. Patent No. 4,883,750; Qbeta Replicase, described in PCT Intl. Pat. Appl. Publ. No. PCT/US87/00880; Strand Displacement Amplification (SDA) and Repair Chain Reaction (RCR). Still other amplification methods are described in Great Britain Pat. Appl. No. 2 202 328, and in PCT Intl. Pat. Appl. Publ. No. PCT/US89/01025. Other nucleic acid amplification procedures include transcription-based amplification systems (TAS) (PCT Intl. Pat. Appl. Publ. No. WO 88/10315), including nucleic acid sequence based amplification (NASBA) and 3SR. Eur. Pat. Appl. Publ. No. 329,822 describes a nucleic acid amplification process involving cyclically synthesizing single-stranded RNA ("ssRNA"), ssDNA, and double-stranded DNA (dsDNA). PCT Intl. Pat. Appl. Publ. No. WO 89/06700 describes a nucleic acid sequence amplification scheme based on the hybridization of a promoter/primer sequence to a target single-stranded DNA ("ssDNA") followed by transcription of many RNA copies of the sequence. Other amplification methods such as "RACE" (Frohman, 1990), and "one-sided PCR" (Ohara, 1989) are also well-known to those of skill in the art.

An amplified portion of a polynucleotide of the present invention may be used to isolate a full length gene from a suitable library (e.g., a tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed

libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or
5 bacteriophage library is then generally screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may
10 be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences can
15 then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, amplification techniques, such as those described above, can be useful for obtaining a full length coding sequence from a partial cDNA sequence. One such amplification technique is inverse PCR (see Triglia et al., *Nucl. Acids Res.* 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a
25 known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or
30 RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5'

and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic.* 1:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res.* 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

5 In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences
10 may also be obtained by analysis of genomic fragments.

In other embodiments of the invention, polynucleotide sequences or fragments thereof which encode polypeptides of the invention, or fusion proteins or functional equivalents thereof, may be used in recombinant DNA molecules to direct expression of a polypeptide in appropriate host cells. Due to the inherent degeneracy of
15 the genetic code, other DNA sequences that encode substantially the same or a functionally equivalent amino acid sequence may be produced and these sequences may be used to clone and express a given polypeptide.

As will be understood by those of skill in the art, it may be advantageous in some instances to produce polypeptide-encoding nucleotide sequences possessing
20 non-naturally occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce a recombinant RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring sequence.

25 Moreover, the polynucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter polypeptide encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the gene product. For example, DNA shuffling by random fragmentation and PCR reassembly of gene
30 fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. In addition, site-directed mutagenesis may be used to insert new restriction

sites, alter glycosylation patterns, change codon preference, produce splice variants, or introduce mutations, and so forth.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences may be ligated to a heterologous sequence to 5 encode a fusion protein. For example, to screen peptide libraries for inhibitors of polypeptide activity, it may be useful to encode a chimeric protein that can be recognized by a commercially available antibody. A fusion protein may also be engineered to contain a cleavage site located between the polypeptide-encoding sequence and the heterologous protein sequence, so that the polypeptide may be cleaved 10 and purified away from the heterologous moiety.

Sequences encoding a desired polypeptide may be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers, M. H. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 215-223, Horn, T. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 225-232). Alternatively, the protein itself may be produced using chemical 15 methods to synthesize the amino acid sequence of a polypeptide, or a portion thereof. For example, peptide synthesis can be performed using various solid-phase techniques (Roberge, J. Y. et al. (1995) *Science* 269:202-204) and automated synthesis may be achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin Elmer, Palo Alto, CA).

20 A newly synthesized peptide may be substantially purified by preparative high performance liquid chromatography (e.g., Creighton, T. (1983) Proteins, Structures and Molecular Principles, WH Freeman and Co., New York, N.Y.) or other comparable techniques available in the art. The composition of the synthetic peptides may be confirmed by amino acid analysis or sequencing (e.g., the Edman 25 degradation procedure). Additionally, the amino acid sequence of a polypeptide, or any part thereof, may be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

In order to express a desired polypeptide, the nucleotide sequences 30 encoding the polypeptide, or functional equivalents, may be inserted into appropriate expression vector, i.e., a vector which contains the necessary elements for the

transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art may be used to construct expression vectors containing sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Such techniques are described, for example, in Sambrook, J. et al. (1989) Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. et al. (1989) Current Protocols in Molecular Biology, John Wiley & Sons, New York, N.Y.

A variety of expression vector/host systems may be utilized to contain 10 and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with virus expression vectors (e.g., baculovirus); plant cell systems transformed with virus expression vectors (e.g., cauliflower mosaic virus, 15 CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems.

The "control elements" or "regulatory sequences" present in an expression vector are those non-translated regions of the vector--enhancers, promoters, 5' and 3' untranslated regions--which interact with host cellular proteins to carry out 20 transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used. For example, when cloning in bacterial systems, inducible promoters such as the hybrid lacZ promoter of the pBLUESCRIPT phagemid (Stratagene, La Jolla, Calif.) or 25 pSPORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like may be used. In mammalian cell systems, promoters from mammalian genes or from mammalian viruses are generally preferred. If it is necessary to generate a cell line that contains multiple copies of the sequence encoding a polypeptide, vectors based on SV40 or EBV may be advantageously used with an appropriate selectable marker.

In bacterial systems, any of a number of expression vectors may be 30 selected depending upon the use intended for the expressed polypeptide. For example,

when large quantities are needed, for example for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be used. Such vectors include, but are not limited to, the multifunctional *E. coli* cloning and expression vectors such as pBLUESCRIPT (Stratagene), in which the sequence 5 encoding the polypeptide of interest may be ligated into the vector in frame with sequences for the amino-terminal Met and the subsequent 7 residues of .beta.-galactosidase so that a hybrid protein is produced; pIN vectors (Van Heeke, G. and S. M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509); and the like. pGEX Vectors (Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion 10 proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose beads followed by elution in the presence of free glutathione. Proteins made in such systems may be designed to include heparin, thrombin, or factor XA protease cleavage sites so that the cloned polypeptide of interest can be released from the GST moiety at 15 will.

In the yeast, *Saccharomyces cerevisiae*, a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH may be used. For reviews, see Ausubel et al. (supra) and Grant et al. (1987) *Methods Enzymol.* 153:516-544.

20 In cases where plant expression vectors are used, the expression of sequences encoding polypeptides may be driven by any of a number of promoters. For example, viral promoters such as the 35S and 19S promoters of CaMV may be used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. (1987) *EMBO J.* 6:307-311. Alternatively, plant promoters such as the small subunit of 25 RUBISCO or heat shock promoters may be used (Coruzzi, G. et al. (1984) *EMBO J.* 3:1671-1680; Broglie, R. et al. (1984) *Science* 224:838-843; and Winter, J. et al. (1991) *Results Probl. Cell Differ.* 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques are described in a number of generally available reviews (see, for example, Hobbs, S. or 30 Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

An insect system may also be used to express a polypeptide of interest. For example, in one such system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The sequences encoding the polypeptide may be cloned into a 5 non-essential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein. The recombinant viruses may then be used to infect, for example, *S. frugiperda* cells or *Trichoplusia* larvae in which the polypeptide of interest may be expressed 10 (Engelhard, E. K. et al. (1994) *Proc. Natl. Acad. Sci.* 91 :3224-3227).

In mammalian host cells, a number of viral-based expression systems are generally available. For example, in cases where an adenovirus is used as an expression vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader 15 sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus which is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) *Proc. Natl. Acad. Sci.* 81:3655-3659). In addition, transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

20 Specific initiation signals may also be used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control 25 signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous translational control signals including the ATG initiation codon should be provided. Furthermore, the initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. 30 The efficiency of expression may be enhanced by the inclusion of enhancers which are

appropriate for the particular cell system which is used, such as those described in the literature (Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162).

In addition, a host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the 5 desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to facilitate correct insertion, folding and/or function. Different host cells such as CHO, COS, HeLa, MDCK, HEK293, and WI38, which have specific cellular 10 machinery and characteristic mechanisms for such post-translational activities, may be chosen to ensure the correct modification and processing of the foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines which stably express a polynucleotide of interest may be transformed using expression vectors which may 15 contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which 20 successfully express the introduced sequences. Resistant clones of stably transformed cells may be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler, M. et al. (1977) *Cell* 11:223-32) and adenine phosphoribosyltransferase 25 (Lowy, I. et al. (1990) *Cell* 22:817-23) genes which can be employed in tk.sup.- or apt.sup.- cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, dhfr which confers resistance to methotrexate (Wigler, M. et al. (1980) *Proc. Natl. Acad. Sci.* 77:3567-70); npt, which confers resistance to the aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. et 30 al (1981) *J. Mol. Biol.* 150:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*).

Additional selectable genes have been described, for example, trpB, which allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in place of histidine (Hartman, S. C. and R. C. Mulligan (1988) *Proc. Natl. Acad. Sci.* 85:8047-51). The use of visible markers has gained popularity with such markers as 5 anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. et al. (1995) *Methods Mol. Biol.* 55:121-131).

Although the presence/absence of marker gene expression suggests that 10 the gene of interest is also present, its presence and expression may need to be confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a polypeptide-encoding sequence under the control of a single promoter. 15 Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

Alternatively, host cells that contain and express a desired polynucleotide sequence may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA- 20 RNA hybridizations and protein bioassay or immunoassay techniques which include, for example, membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

A variety of protocols for detecting and measuring the expression of 25 polynucleotide-encoded products, using either polyclonal or monoclonal antibodies specific for the product are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on a given polypeptide may be preferred for some applications, but a competitive binding assay may also be employed. 30 These and other assays are described, among other places, in Hampton, R. et al. (1990;

Serological Methods, a Laboratory Manual, APS Press, St Paul. Minn.) and Maddox, D. E. et al. (1983; *J. Exp. Med.* 158:1211-1216).

A wide variety of labels and conjugation techniques are known by those skilled in the art and may be used in various nucleic acid and amino acid assays. Means 5 for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR amplification using a labeled nucleotide. Alternatively, the sequences, or any portions thereof may be cloned into a vector for the production of an mRNA probe. Such vectors are known in the art, are commercially available, and may be used to synthesize RNA 10 probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which may be used include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

15 Host cells transformed with a polynucleotide sequence of interest may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be secreted or contained intracellularly depending on the sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing polynucleotides of the 20 invention may be designed to contain signal sequences which direct secretion of the encoded polypeptide through a prokaryotic or eukaryotic cell membrane. Other recombinant constructions may be used to join sequences encoding a polypeptide of interest to nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are 25 not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen, San Diego, 30 Calif.) between the purification domain and the encoded polypeptide may be used to facilitate purification. One such expression vector provides for expression of a fusion

protein containing a polypeptide of interest and a nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. et al. (1992, *Prot. Exp. Purif.* 3:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors which contain fusion proteins is provided in Kroll, D. J. et al. (1993; *DNA Cell Biol.* 12:441-453).

In addition to recombinant production methods, polypeptides of the invention, and fragments thereof, may be produced by direct peptide synthesis using solid-phase techniques (Merrifield J. (1963) *J. Am. Chem. Soc.* 85:2149-2154). Protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Alternatively, various fragments may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.

Antibody Compositions, Fragments Thereof and Other Binding Agents

According to another aspect, the present invention further provides binding agents, such as antibodies and antigen-binding fragments thereof, that exhibit immunological binding to a tumor polypeptide disclosed herein, or to a portion, variant or derivative thereof. An antibody, or antigen-binding fragment thereof, is said to "specifically bind," "immunologically bind," and/or is "immunologically reactive" to a polypeptide of the invention if it reacts at a detectable level (within, for example, an ELISA assay) with the polypeptide, and does not react detectably with unrelated polypeptides under similar conditions.

Immunological binding, as used in this context, generally refers to the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific. The strength, or affinity of immunological binding interactions can be expressed in terms of the dissociation constant (K_d) of the interaction, wherein a smaller K_d represents a greater affinity. Immunological binding properties of selected polypeptides can be quantified

using methods well known in the art. One such method entails measuring the rates of antigen-binding site/antigen complex formation and dissociation, wherein those rates depend on the concentrations of the complex partners, the affinity of the interaction, and on geometric parameters that equally influence the rate in both directions. Thus, both 5 the "on rate constant" (K_{on}) and the "off rate constant" (K_{off}) can be determined by calculation of the concentrations and the actual rates of association and dissociation. The ratio of K_{off}/K_{on} enables cancellation of all parameters not related to affinity, and is thus equal to the dissociation constant K_d . See, generally, Davies et al. (1990) Annual Rev. Biochem. 59:439-473.

10 An "antigen-binding site," or "binding portion" of an antibody refers to the part of the immunoglobulin molecule that participates in antigen binding. The antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains are referred to as "hypervariable 15 regions" which are interposed between more conserved flanking stretches known as "framework regions," or "FRs". Thus the term "FR" refers to amino acid sequences which are naturally found between and adjacent to hypervariable regions in immunoglobulins. In an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each 20 other in three dimensional space to form an antigen-binding surface. The antigen-binding surface is complementary to the three-dimensional surface of a bound antigen, and the three hypervariable regions of each of the heavy and light chains are referred to as "complementarity-determining regions," or "CDRs."

Binding agents may be further capable of differentiating between 25 patients with and without a cancer, such as pancreatic cancer, using the representative assays provided herein. For example, antibodies or other binding agents that bind to a tumor protein will preferably generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, more preferably at least about 30% of patients. Alternatively, or in addition, the antibody will generate a negative signal 30 indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological

samples (*e.g.*, blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. Preferably, a statistically significant number of samples with and without the disease 5 will be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, 10 an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation 15 of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the 20 immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled 25 periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. 30 Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the

desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized 5 animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, 10 colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the 15 yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process 20 in, for example, an affinity chromatography step.

A number of therapeutically useful molecules are known in the art which comprise antigen-binding sites that are capable of exhibiting immunological binding properties of an antibody molecule. The proteolytic enzyme papain preferentially cleaves IgG molecules to yield several fragments, two of which (the "F(ab)" fragments) 25 each comprise a covalent heterodimer that includes an intact antigen-binding site. The enzyme pepsin is able to cleave IgG molecules to provide several fragments, including the "F(ab')₂" fragment which comprises both antigen-binding sites. An "Fv" fragment can be produced by preferential proteolytic cleavage of an IgM, and on rare occasions IgG or IgA immunoglobulin molecule. Fv fragments are, however, more commonly 30 derived using recombinant techniques known in the art. The Fv fragment includes a non-covalent V_H::V_L heterodimer including an antigen-binding site which retains much

of the antigen recognition and binding capabilities of the native antibody molecule. Inbar et al. (1972) Proc. Nat. Acad. Sci. USA 69:2659-2662; Hochman et al. (1976) Biochem 15:2706-2710; and Ehrlich et al. (1980) Biochem 19:4091-4096.

A single chain Fv ("sFv") polypeptide is a covalently linked V_H:V_L heterodimer which is expressed from a gene fusion including V_H- and V_L-encoding genes linked by a peptide-encoding linker. Huston et al. (1988) Proc. Nat. Acad. Sci. USA 85(16):5879-5883. A number of methods have been described to discern chemical structures for converting the naturally aggregated--but chemically separated--light and heavy polypeptide chains from an antibody V region into an sFv molecule which will 10 fold into a three dimensional structure substantially similar to the structure of an antigen-binding site. See, e.g., U.S. Pat. Nos. 5,091,513 and 5,132,405, to Huston et al.; and U.S. Pat. No. 4,946,778, to Ladner et al.

Each of the above-described molecules includes a heavy chain and a light chain CDR set, respectively interposed between a heavy chain and a light chain 15 FR set which provide support to the CDRS and define the spatial relationship of the CDRs relative to each other. As used herein, the term "CDR set" refers to the three hypervariable regions of a heavy or light chain V region. Proceeding from the N-terminus of a heavy or light chain, these regions are denoted as "CDR1," "CDR2," and "CDR3" respectively. An antigen-binding site, therefore, includes six CDRs, comprising 20 the CDR set from each of a heavy and a light chain V region. A polypeptide comprising a single CDR, (e.g., a CDR1, CDR2 or CDR3) is referred to herein as a "molecular recognition unit." Crystallographic analysis of a number of antigen-antibody complexes has demonstrated that the amino acid residues of CDRs form extensive contact with bound antigen, wherein the most extensive antigen contact is with the heavy chain 25 CDR3. Thus, the molecular recognition units are primarily responsible for the specificity of an antigen-binding site.

As used herein, the term "FR set" refers to the four flanking amino acid sequences which frame the CDRs of a CDR set of a heavy or light chain V region. Some FR residues may contact bound antigen; however, FRs are primarily responsible 30 for folding the V region into the antigen-binding site, particularly the FR residues directly adjacent to the CDRS. Within FRs, certain amino residues and certain structural

features are very highly conserved. In this regard, all V region sequences contain an internal disulfide loop of around 90 amino acid residues. When the V regions fold into a binding-site, the CDRs are displayed as projecting loop motifs which form an antigen-binding surface. It is generally recognized that there are conserved structural regions of 5 FRs which influence the folded shape of the CDR loops into certain "canonical" structures--regardless of the precise CDR amino acid sequence. Further, certain FR residues are known to participate in non-covalent interdomain contacts which stabilize the interaction of the antibody heavy and light chains.

A number of "humanized" antibody molecules comprising an antigen-
10 binding site derived from a non-human immunoglobulin have been described, including chimeric antibodies having rodent V regions and their associated CDRs fused to human constant domains (Winter et al. (1991) Nature 349:293-299; Lobuglio et al. (1989) Proc. Nat. Acad. Sci. USA 86:4220-4224; Shaw et al. (1987) J Immunol. 138:4534-4538; and Brown et al. (1987) Cancer Res. 47:3577-3583), rodent CDRs grafted into a
15 human supporting FR prior to fusion with an appropriate human antibody constant domain (Riechmann et al. (1988) Nature 332:323-327; Verhoeyen et al. (1988) Science 239:1534-1536; and Jones et al. (1986) Nature 321:522-525), and rodent CDRs supported by recombinantly veneered rodent FRs (European Patent Publication No. 519,596, published Dec. 23, 1992). These "humanized" molecules are designed to
20 minimize unwanted immunological response toward rodent antihuman antibody molecules which limits the duration and effectiveness of therapeutic applications of those moieties in human recipients.

As used herein, the terms "veneered FRs" and "recombinantly veneered FRs" refer to the selective replacement of FR residues from, e.g., a rodent heavy or light
25 chain V region, with human FR residues in order to provide a xenogeneic molecule comprising an antigen-binding site which retains substantially all of the native FR polypeptide folding structure. Veneering techniques are based on the understanding that the ligand binding characteristics of an antigen-binding site are determined primarily by the structure and relative disposition of the heavy and light chain CDR sets within the
30 antigen-binding surface. Davies et al. (1990) Ann. Rev. Biochem. 59:439-473. Thus, antigen binding specificity can be preserved in a humanized antibody only wherein the

CDR structures, their interaction with each other, and their interaction with the rest of the V region domains are carefully maintained. By using veneering techniques, exterior (e.g., solvent-accessible) FR residues which are readily encountered by the immune system are selectively replaced with human residues to provide a hybrid molecule that 5 comprises either a weakly immunogenic, or substantially non-immunogenic veneered surface.

The process of veneering makes use of the available sequence data for human antibody variable domains compiled by Kabat et al., in Sequences of Proteins of Immunological Interest, 4th ed., (U.S. Dept. of Health and Human Services, U.S. 10 Government Printing Office, 1987), updates to the Kabat database, and other accessible U.S. and foreign databases (both nucleic acid and protein). Solvent accessibilities of V region amino acids can be deduced from the known three-dimensional structure for human and murine antibody fragments. There are two general steps in veneering a murine antigen-binding site. Initially, the FRs of the variable domains of an antibody 15 molecule of interest are compared with corresponding FR sequences of human variable domains obtained from the above-identified sources. The most homologous human V regions are then compared residue by residue to corresponding murine amino acids. The residues in the murine FR which differ from the human counterpart are replaced by the residues present in the human moiety using recombinant techniques well known in the 20 art. Residue switching is only carried out with moieties which are at least partially exposed (solvent accessible), and care is exercised in the replacement of amino acid residues which may have a significant effect on the tertiary structure of V region domains, such as proline, glycine and charged amino acids.

In this manner, the resultant "veneered" murine antigen-binding sites are 25 thus designed to retain the murine CDR residues, the residues substantially adjacent to the CDRs, the residues identified as buried or mostly buried (solvent inaccessible), the residues believed to participate in non-covalent (e.g., electrostatic and hydrophobic) contacts between heavy and light chain domains, and the residues from conserved structural regions of the FRs which are believed to influence the "canonical" tertiary 30 structures of the CDR loops. These design criteria are then used to prepare recombinant nucleotide sequences which combine the CDRs of both the heavy and light chain of a

murine antigen-binding site into human-appearing FRs that can be used to transfect mammalian cells for the expression of recombinant human antibodies which exhibit the antigen specificity of the murine antibody molecule.

In another embodiment of the invention, monoclonal antibodies of the 5 present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ⁹⁰Y, ¹²³I, ¹²⁵I, ¹³¹I, ¹⁸⁶Re, ¹⁸⁸Re, ²¹¹At, and ²¹²Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins 10 include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a 15 substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulphydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an 20 antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which 25 otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, 30 sulphydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the 5 intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitzer), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell 10 et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent 15 may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as 20 albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating 25 compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating 30 compounds and their synthesis.

T Cell Compositions

The present invention, in another aspect, provides T cells specific for a tumor polypeptide disclosed herein, or for a variant or derivative thereof. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example,

5 T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. (Irvine, CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or

10 unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a polypeptide, polynucleotide encoding a polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide of interest. Preferably, a

15 tumor polypeptide or polynucleotide of the invention is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a polypeptide of the present invention if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chem et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the

20 proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.*, by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7

25 days will typically result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as

30

measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN- γ) is indicative of T cell activation (see Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a tumor polypeptide, polynucleotide or 5 polypeptide-expressing APC may be CD4 $^{+}$ and/or CD8 $^{+}$. Tumor polypeptide-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4 $^{+}$ or CD8 $^{+}$ T cells that proliferate in 10 response to a tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator 15 cells that synthesize a tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of the tumor polypeptide can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

T Cell Receptor Compositions

20 The T cell receptor (TCR) consists of 2 different, highly variable polypeptide chains, termed the T-cell receptor α and β chains, that are linked by a disulfide bond (Janeway, Travers, Walport. Immunobiology. Fourth Ed., 148-159. Elsevier Science Ltd/Garland Publishing. 1999). The α/β heterodimer complexes with the invariant CD3 chains at the cell membrane. This complex recognizes specific 25 antigenic peptides bound to MHC molecules. The enormous diversity of TCR specificities is generated much like immunoglobulin diversity, through somatic gene rearrangement. The β chain genes contain over 50 variable (V), 2 diversity (D), over 10 joining (J) segments, and 2 constant region segments (C). The α chain genes contain over 70 V segments, and over 60 J segments but no D segments, as well as one C segment. During T cell development in the thymus, the D to J gene rearrangement of 30

the β chain occurs, followed by the V gene segment rearrangement to the DJ. This functional VDJ β exon is transcribed and spliced to join to a C β . For the α chain, a V α gene segment rearranges to a J α gene segment to create the functional exon that is then transcribed and spliced to the C α . Diversity is further increased during the 5 recombination process by the random addition of P and N-nucleotides between the V, D, and J segments of the β chain and between the V and J segments in the α chain (Janeway, Travers, Walport. Immunobiology. Fourth Ed., 98 and 150. Elsevier Science Ltd/Garland Publishing, 1999).

The present invention, in another aspect, provides TCRs specific for a 10 polypeptide disclosed herein, or for a variant or derivative thereof. In accordance with the present invention, polynucleotide and amino acid sequences are provided for the V-J or V-D-J junctional regions or parts thereof for the alpha and beta chains of the T-cell receptor which recognize tumor polypeptides described herein. In general, this aspect of the invention relates to T-cell receptors which recognize or bind tumor polypeptides 15 presented in the context of MHC. In a preferred embodiment the tumor antigens recognized by the T-cell receptors comprise a polypeptide of the present invention. For example, cDNA encoding a TCR specific for a pancreatic tumor peptide can be isolated from T cells specific for a tumor polypeptide using standard molecular biological and recombinant DNA techniques.

20 This invention further includes the T-cell receptors or analogs thereof having substantially the same function or activity as the T-cell receptors of this invention which recognize or bind tumor polypeptides. Such receptors include, but are not limited to, a fragment of the receptor, or a substitution, addition or deletion mutant of a T-cell receptor provided herein. This invention also encompasses polypeptides or 25 peptides that are substantially homologous to the T-cell receptors provided herein or that retain substantially the same activity. The term "analog" includes any protein or polypeptide having an amino acid residue sequence substantially identical to the T-cell receptors provided herein in which one or more residues, preferably no more than 5 residues, more preferably no more than 25 residues have been conservatively 30 substituted with a functionally similar residue and which displays the functional aspects of the T-cell receptor as described herein.

The present invention further provides for suitable mammalian host cells, for example, non-specific T cells, that are transfected with a polynucleotide encoding TCRs specific for a polypeptide described herein, thereby rendering the host cell specific for the polypeptide. The α and β chains of the TCR may be contained on 5 separate expression vectors or alternatively, on a single expression vector that also contains an internal ribosome entry site (IRES) for cap-independent translation of the gene downstream of the IRES. Said host cells expressing TCRs specific for the polypeptide may be used, for example, for adoptive immunotherapy of pancreatic cancer as discussed further below.

10 In further aspects of the present invention, cloned TCRs specific for a polypeptide recited herein may be used in a kit for the diagnosis of pancreatic cancer. For example, the nucleic acid sequence or portions thereof, of tumor-specific TCRs can be used as probes or primers for the detection of expression of the rearranged genes encoding the specific TCR in a biological sample. Therefore, the present invention 15 further provides for an assay for detecting messenger RNA or DNA encoding the TCR specific for a polypeptide.

Pharmaceutical Compositions

In additional embodiments, the present invention concerns formulation of one or more of the polynucleotide, polypeptide, T-cell, TCR, and/or antibody 20 compositions disclosed herein in pharmaceutically-acceptable carriers for administration to a cell or an animal, either alone, or in combination with one or more other modalities of therapy.

It will be understood that, if desired, a composition as disclosed herein may be administered in combination with other agents as well, such as, e.g., other 25 proteins or polypeptides or various pharmaceutically-active agents. In fact, there is virtually no limit to other components that may also be included, given that the additional agents do not cause a significant adverse effect upon contact with the target cells or host tissues. The compositions may thus be delivered along with various other agents as required in the particular instance. Such compositions may be purified from 30 host cells or other biological sources, or alternatively may be chemically synthesized as

described herein. Likewise, such compositions may further comprise substituted or derivatized RNA or DNA compositions.

Therefore, in another aspect of the present invention, pharmaceutical compositions are provided comprising one or more of the polynucleotide, polypeptide, 5 antibody, TCR, and/or T-cell compositions described herein in combination with a physiologically acceptable carrier. In certain preferred embodiments, the pharmaceutical compositions of the invention comprise immunogenic polynucleotide and/or polypeptide compositions of the invention for use in prophylactic and therapeutic vaccine applications. Vaccine preparation is generally described in, for example, M.F. 10 Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Generally, such compositions will comprise one or more polynucleotide and/or polypeptide compositions of the present invention in combination with one or more immunostimulants.

It will be apparent that any of the pharmaceutical compositions described 15 herein can contain pharmaceutically acceptable salts of the polynucleotides and polypeptides of the invention. Such salts can be prepared, for example, from pharmaceutically acceptable non-toxic bases, including organic bases (e.g., salts of primary, secondary and tertiary amines and basic amino acids) and inorganic bases (e.g., sodium, potassium, lithium, ammonium, calcium and magnesium salts).

20 In another embodiment, illustrative immunogenic compositions, e.g., vaccine compositions, of the present invention comprise DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the polynucleotide may be administered within any of a variety of delivery systems known to those of ordinary skill in the art. Indeed, numerous gene delivery 25 techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein. Appropriate polynucleotide expression systems will, of course, contain the necessary regulatory DNA regulatory sequences for expression in a patient (such as a suitable promoter and terminating signal). Alternatively, bacterial delivery systems may involve 30 the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope.

Therefore, in certain embodiments, polynucleotides encoding immunogenic polypeptides described herein are introduced into suitable mammalian host cells for expression using any of a number of known viral-based systems. In one illustrative embodiment, retroviruses provide a convenient and effective platform for gene delivery systems. A selected nucleotide sequence encoding a polypeptide of the present invention can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to a subject. A number of illustrative retroviral systems have been described (e.g., U.S. Pat. No. 5,219,740; Miller and Rosman (1989) *BioTechniques* 7:980-990; Miller, A. D. (1990) *Human Gene Therapy* 1:5-14; Scarpa et al. (1991) *Virology* 180:849-852; Burns et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:8033-8037; and Boris-Lawrie and Temin (1993) *Cur. Opin. Genet. Develop.* 3:102-109.

In addition, a number of illustrative adenovirus-based systems have also been described. Unlike retroviruses which integrate into the host genome, adenoviruses persist extrachromosomally thus minimizing the risks associated with insertional mutagenesis (Haj-Ahmad and Graham (1986) *J. Virol.* 57:267-274; Bett et al. (1993) *J. Virol.* 67:5911-5921; Mittereder et al. (1994) *Human Gene Therapy* 5:717-729; Seth et al. (1994) *J. Virol.* 68:933-940; Barr et al. (1994) *Gene Therapy* 1:51-58; Berkner, K. L. (1988) *BioTechniques* 6:616-629; and Rich et al. (1993) *Human Gene Therapy* 4:461-476).

Various adeno-associated virus (AAV) vector systems have also been developed for polynucleotide delivery. AAV vectors can be readily constructed using techniques well known in the art. See, e.g., U.S. Pat. Nos. 5,173,414 and 5,139,941; International Publication Nos. WO 92/01070 and WO 93/03769; Lebkowski et al. (1988) *Molec. Cell. Biol.* 8:3988-3996; Vincent et al. (1990) *Vaccines* 90 (Cold Spring Harbor Laboratory Press); Carter, B. J. (1992) *Current Opinion in Biotechnology* 3:533-539; Muzychka, N. (1992) *Current Topics in Microbiol. and Immunol.* 158:97-129; Kotin, R. M. (1994) *Human Gene Therapy* 5:793-801; Shelling and Smith (1994) *Gene Therapy* 1:165-169; and Zhou et al. (1994) *J. Exp. Med.* 179:1867-1875.

Additional viral vectors useful for delivering the polynucleotides encoding polypeptides of the present invention by gene transfer include those derived

from the pox family of viruses, such as vaccinia virus and avian poxvirus. By way of example, vaccinia virus recombinants expressing the novel molecules can be constructed as follows. The DNA encoding a polypeptide is first inserted into an appropriate vector so that it is adjacent to a vaccinia promoter and flanking vaccinia 5 DNA sequences, such as the sequence encoding thymidine kinase (TK). This vector is then used to transfect cells which are simultaneously infected with vaccinia. Homologous recombination serves to insert the vaccinia promoter plus the gene encoding the polypeptide of interest into the viral genome. The resulting TK.sup.(-) recombinant can be selected by culturing the cells in the presence of 5- 10 bromodeoxyuridine and picking viral plaques resistant thereto.

A vaccinia-based infection/transfection system can be conveniently used to provide for inducible, transient expression or coexpression of one or more polypeptides described herein in host cells of an organism. In this particular system, cells are first infected *in vitro* with a vaccinia virus recombinant that encodes the 15 bacteriophage T7 RNA polymerase. This polymerase displays exquisite specificity in that it only transcribes templates bearing T7 promoters. Following infection, cells are transfected with the polynucleotide or polynucleotides of interest, driven by a T7 promoter. The polymerase expressed in the cytoplasm from the vaccinia virus recombinant transcribes the transfected DNA into RNA which is then translated into 20 polypeptide by the host translational machinery. The method provides for high level, transient, cytoplasmic production of large quantities of RNA and its translation products. See, e.g., Elroy-Stein and Moss, Proc. Natl. Acad. Sci. USA (1990) 87:6743-6747; Fuerst et al. Proc. Natl. Acad. Sci. USA (1986) 83:8122-8126.

Alternatively, avipoxviruses, such as the fowlpox and canarypox viruses, 25 can also be used to deliver the coding sequences of interest. Recombinant avipox viruses, expressing immunogens from mammalian pathogens, are known to confer protective immunity when administered to non-avian species. The use of an Avipox vector is particularly desirable in human and other mammalian species since members of the Avipox genus can only productively replicate in susceptible avian species and 30 therefore are not infective in mammalian cells. Methods for producing recombinant Avipoxviruses are known in the art and employ genetic recombination, as described

above with respect to the production of vaccinia viruses. See, e.g., WO 91/12882; WO 89/03429; and WO 92/03545.

Any of a number of alphavirus vectors can also be used for delivery of polynucleotide compositions of the present invention, such as those vectors described in 5 U.S. Patent Nos. 5,843,723; 6,015,686; 6,008,035 and 6,015,694. Certain vectors based on Venezuelan Equine Encephalitis (VEE) can also be used, illustrative examples of which can be found in U.S. Patent Nos. 5,505,947 and 5,643,576.

Moreover, molecular conjugate vectors, such as the adenovirus chimeric vectors described in Michael et al. *J. Biol. Chem.* (1993) 268:6866-6869 and Wagner et 10 al. *Proc. Natl. Acad. Sci. USA* (1992) 89:6099-6103, can also be used for gene delivery under the invention.

Additional illustrative information on these and other known viral-based delivery systems can be found, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner 15 et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science* 252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; 20 and Guzman et al., *Cir. Res.* 73:1202-1207, 1993.

In certain embodiments, a polynucleotide may be integrated into the genome of a target cell. This integration may be in the specific location and orientation via homologous recombination (gene replacement) or it may be integrated in a random, non-specific location (gene augmentation). In yet further embodiments, the 25 polynucleotide may be stably maintained in the cell as a separate, episomal segment of DNA. Such polynucleotide segments or "episomes" encode sequences sufficient to permit maintenance and replication independent of or in synchronization with the host cell cycle. The manner in which the expression construct is delivered to a cell and where in the cell the polynucleotide remains is dependent on the type of expression 30 construct employed.

In another embodiment of the invention, a polynucleotide is administered/delivered as "naked" DNA, for example as described in Ulmer et al., *Science* 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable 5 beads, which are efficiently transported into the cells.

In still another embodiment, a composition of the present invention can be delivered via a particle bombardment approach, many of which have been described. In one illustrative example, gas-driven particle acceleration can be achieved with devices such as those manufactured by Powderject Pharmaceuticals PLC (Oxford, UK) 10 and Powderject Vaccines Inc. (Madison, WI), some examples of which are described in U.S. Patent Nos. 5,846,796; 6,010,478; 5,865,796; 5,584,807; and EP Patent No. 0500 799. This approach offers a needle-free delivery approach wherein a dry powder formulation of microscopic particles, such as polynucleotide or polypeptide particles, are accelerated to high speed within a helium gas jet generated by a hand held device, 15 propelling the particles into a target tissue of interest.

In a related embodiment, other devices and methods that may be useful for gas-driven needle-less injection of compositions of the present invention include those provided by Bioject, Inc. (Portland, OR), some examples of which are described in U.S. Patent Nos. 4,790,824; 5,064,413; 5,312,335; 5,383,851; 5,399,163; 5,520,639 20 and 5,993,412.

According to another embodiment, the pharmaceutical compositions described herein will comprise one or more immunostimulants in addition to the immunogenic polynucleotide, polypeptide, antibody, T-cell, TCR, and/or APC compositions of this invention. An immunostimulant refers to essentially any substance 25 that enhances or potentiates an immune response (antibody and/or cell-mediated) to an exogenous antigen. One preferred type of immunostimulant comprises an adjuvant. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived 30 proteins. Certain adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck

Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; 5 polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

- Within certain embodiments of the invention, the adjuvant composition is preferably one that induces an immune response predominantly of the Th1 type.
- 10 High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2- 15 type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.
- 20 Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A, together with an aluminum salt. MPL® adjuvants are available from Corixa Corporation (Seattle, WA; see, for example, US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing 25 oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant comprises a saponin, 30 such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or *Gypsophila* or

Chenopodium quinoa saponins. Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example combinations of at least two of the following group comprising QS21, QS7, Quil A, β -escin, or digitonin.

- 5 Alternatively the saponin formulations may be combined with vaccine vehicles composed of chitosan or other polycationic polymers, polylactide and polylactide-co-glycolide particles, poly-N-acetyl glucosamine-based polymer matrix, particles composed of polysaccharides or chemically modified polysaccharides, liposomes and lipid-based particles, particles composed of glycerol monoesters, etc.
- 10 The saponins may also be formulated in the presence of cholesterol to form particulate structures such as liposomes or ISCOMs. Furthermore, the saponins may be formulated together with a polyoxyethylene ether or ester, in either a non-particulate solution or suspension, or in a particulate structure such as a paucilamellar liposome or ISCOM. The saponins may also be formulated with excipients such as Carbopol[®] to increase
- 15 viscosity, or may be formulated in a dry powder form with a powder excipient such as lactose.

- In one preferred embodiment, the adjuvant system includes the combination of a monophosphoryl lipid A and a saponin derivative, such as the combination of QS21 and 3D-MPL[®] adjuvant, as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. Another particularly preferred adjuvant formulation employing QS21, 3D-MPL[®] adjuvant and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

- 25 Another enhanced adjuvant system involves the combination of a CpG-containing oligonucleotide and a saponin derivative particularly the combination of CpG and QS21 is disclosed in WO 00/09159. Preferably the formulation additionally comprises an oil in water emulsion and tocopherol.

- 30 Additional illustrative adjuvants for use in the pharmaceutical compositions of the invention include Montanide ISA 720 (Seppic, France), SAF (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series

of adjuvants (e.g., SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Enhazyne[®]) (Corixa, Hamilton, MT), RC-529 (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, 5 the disclosures of which are incorporated herein by reference in their entireties, and polyoxyethylene ether adjuvants such as those described in WO 99/52549A1.

Other preferred adjuvants include adjuvant molecules of the general formula



10 wherein, n is 1-50, A is a bond or $-\text{C}(\text{O})-$, R is C₁₋₅₀ alkyl or Phenyl C₁₋₅₀ alkyl.

One embodiment of the present invention consists of a vaccine formulation comprising a polyoxyethylene ether of general formula (I), wherein n is between 1 and 50, preferably 4-24, most preferably 9; the R component is C₁₋₅₀, preferably C₄-C₂₀ alkyl and most preferably C₁₂ alkyl, and A is a bond. The 15 concentration of the polyoxyethylene ethers should be in the range 0.1-20%, preferably from 0.1-10%, and most preferably in the range 0.1-1%. Preferred polyoxyethylene ethers are selected from the following group: polyoxyethylene-9-lauryl ether, polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether. 20 Polyoxyethylene ethers such as polyoxyethylene lauryl ether are described in the Merck index (12th edition: entry 7717). These adjuvant molecules are described in WO 99/52549.

The polyoxyethylene ether according to the general formula (I) above may, if desired, be combined with another adjuvant. For example, a preferred adjuvant 25 combination is preferably with CpG as described in the pending UK patent application GB 9820956.2.

According to another embodiment of this invention, an immunogenic composition described herein is delivered to a host via antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be 30 engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or

maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic
5 or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic
10 antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-
15 surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

20 Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes
25 harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

30 Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized

phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc_y receptor and mannose receptor. The mature 5 phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide of the 10 invention (or portion or other variant thereof) such that the encoded polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a pharmaceutical composition comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be 15 administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or 20 progenitor cells with the tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated 25 immunological partner, separately or in the presence of the polypeptide.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will typically vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, 30 including for example, topical, oral, nasal, mucosal, intravenous, intracranial, intraperitoneal, subcutaneous and intramuscular administration.

Carriers for use within such pharmaceutical compositions are biocompatible, and may also be biodegradable. In certain embodiments, the formulation preferably provides a relatively constant level of active component release. In other embodiments, however, a more rapid rate of release immediately upon 5 administration may be desired. The formulation of such compositions is well within the level of ordinary skill in the art using known techniques. Illustrative carriers useful in this regard include microparticles of poly(lactide-co-glycolide), polyacrylate, latex, starch, cellulose, dextran and the like. Other illustrative delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (e.g., 10 a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (see e.g., U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of 15 the condition to be treated or prevented.

In another illustrative embodiment, biodegradable microspheres (e.g., polylactate polyglycolate) are employed as carriers for the compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763; 20 5,814,344, 5,407,609 and 5,942,252. Modified hepatitis B core protein carrier systems, such as described in WO/99 40934, and references cited therein, will also be useful for many applications. Another illustrative carrier/delivery system employs a carrier comprising particulate-protein complexes, such as those described in U.S. Patent No. 5,928,647, which are capable of inducing a class I-restricted cytotoxic T lymphocyte 25 responses in a host.

In another illustrative embodiment, calcium phosphate core particles are employed as carriers, vaccine adjuvants, or as controlled release matrices for the compositions of this invention. Exemplary calcium phosphate particles are disclosed, for example, in published patent application No. WO/0046147.

30 The pharmaceutical compositions of the invention will often further comprise one or more buffers (e.g., neutral buffered saline or phosphate buffered

saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextran), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (*e.g.*, aluminum hydroxide), solutes that render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a 5 recipient, suspending agents, thickening agents and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate.

The pharmaceutical compositions described hereii may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are typically sealed in such a way to preserve the sterility and stability of the 10 formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

The development of suitable dosing and treatment regimens for using the 15 particular compositions described herein in a variety of treatment regimens, including *e.g.*, oral, parenteral, intravenous, intranasal, and intramuscular administration and formulation, is well known in the art, some of which are briefly discussed below for general purposes of illustration.

In certain applications, the pharmaceutical compositions disclosed herein 20 may be delivered *via* oral administration to an animal. As such, these compositions may be formulated with an inert diluent or with an assimilable edible carrier, or they may be enclosed in hard- or soft-shell gelatin capsule, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet.

The active compounds may even be incorporated with excipients and 25 used in the form of ingestible tablets, buccal tables, troches, capsules, elixirs, suspensions, syrups, wafers, and the like (see, for example, Mathiowitz *et al.*, Nature 1997 Mar 27;386(6623):410-4; Hwang *et al.*, Crit Rev Ther Drug Carrier Syst 1998;15(3):243-84; U. S. Patent 5,641,515; U. S. Patent 5,580,579 and U. S. Patent 5,792,451). Tablets, troches, pills, capsules and the like may also contain any of a 30 variety of additional components, for example, a binder, such as gum tragacanth, acacia, cornstarch, or gelatin; excipients, such as dicalcium phosphate; a disintegrating agent,

such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a sweetening agent, such as sucrose, lactose or saccharin may be added or a flavoring agent, such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar, or both. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition, the active compounds may be incorporated into sustained-release preparation and formulations.

Typically, these formulations will contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 60% or 70% or more of the weight or volume of the total formulation. Naturally, the amount of active compound(s) in each therapeutically useful composition may be prepared is such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated by one skilled in the art of preparing such pharmaceutical formulations, and as such, a variety of dosages and treatment regimens may be desirable.

For oral administration the compositions of the present invention may alternatively be incorporated with one or more excipients in the form of a mouthwash, dentifrice, buccal tablet, oral spray, or sublingual orally-administered formulation. Alternatively, the active ingredient may be incorporated into an oral solution such as one containing sodium borate, glycerin and potassium bicarbonate, or dispersed in a dentifrice, or added in a therapeutically-effective amount to a composition that may include water, binders, abrasives, flavoring agents, foaming agents, and humectants. Alternatively the compositions may be fashioned into a tablet or solution form that may be placed under the tongue or otherwise dissolved in the mouth.

In certain circumstances it will be desirable to deliver the pharmaceutical compositions disclosed herein parenterally, intravenously, intramuscularly, or even

intraperitoneally. Such approaches are well known to the skilled artisan, some of which are further described, for example, in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and U. S. Patent 5,399,363. In certain embodiments, solutions of the active compounds as free base or pharmacologically acceptable salts may be prepared in water suitably 5 mixed with a surfactant, such as hydroxypropylcellulose. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations generally will contain a preservative to prevent the growth of microorganisms.

Illustrative pharmaceutical forms suitable for injectable use include 10 sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions (for example, see U. S. Patent 5,466,468). In all cases the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, 15 such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper fluidity may be maintained, for example, by the use of a coating, such as lecithin, by the maintenance of the required particle size in the case of dispersion and/or 20 by the use of surfactants. The prevention of the action of microorganisms can be facilitated by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in 25 the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

In one embodiment, for parenteral administration in an aqueous solution, the solution should be suitably buffered if necessary and the liquid diluent first rendered isotonic with sufficient saline or glucose. These particular aqueous solutions are 30 especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal administration. In this connection, a sterile aqueous medium that can be employed will

be known to those of skill in the art in light of the present disclosure. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml of hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the subject being treated. Moreover, for human administration, preparations will of course preferably meet sterility, pyrogenicity, and the general safety and purity standards as required by FDA Office of Biologics standards.

In another embodiment of the invention, the compositions disclosed
10 herein may be formulated in a neutral or salt form. Illustrative pharmaceutically-acceptable salts include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be
15 derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective.

20 The carriers can further comprise any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active
25 ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. The phrase "pharmaceutically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human.

In certain embodiments, the pharmaceutical compositions may be
30 delivered by intranasal sprays, inhalation, and/or other aerosol delivery vehicles. Methods for delivering genes, nucleic acids, and peptide compositions directly to the

lungs *via* nasal aerosol sprays has been described, e.g., in U. S. Patent 5,756,353 and U. S. Patent 5,804,212. Likewise, the delivery of drugs using intranasal microparticle resins (Takenaga *et al.*, J Controlled Release 1998 Mar 2;52(1-2):81-7) and lysophosphatidyl-glycerol compounds (U. S. Patent 5,725,871) are also well-known in 5 the pharmaceutical arts. Likewise, illustrative transmucosal drug delivery in the form of a polytetrafluoroethylene support matrix is described in U. S. Patent 5,780,045.

In certain embodiments, liposomes, nanocapsules, microparticles, lipid particles, vesicles, and the like, are used for the introduction of the compositions of the present invention into suitable host cells/organisms. In particular, the compositions of 10 the present invention may be formulated for delivery either encapsulated in a lipid particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like. Alternatively, compositions of the present invention can be bound, either covalently or non-covalently, to the surface of such carrier vehicles.

The formation and use of liposome and liposome-like preparations as 15 potential drug carriers is generally known to those of skill in the art (see for example, Lasic, Trends Biotechnol 1998 Jul;16(7):307-21; Takakura, Nippon Rinsho 1998 Mar;56(3):691-5; Chandran *et al.*, Indian J Exp Biol. 1997 Aug;35(8):801-9; Margalit, Crit Rev Ther Drug Carrier Syst. 1995;12(2-3):233-61; U.S. Patent 5,567,434; U.S. Patent 5,552,157; U.S. Patent 5,565,213; U.S. Patent 5,738,868 and U.S. Patent 20 5,795,587, each specifically incorporated herein by reference in its entirety).

Liposomes have been used successfully with a number of cell types that are normally difficult to transfet by other procedures, including T cell suspensions, primary hepatocyte cultures and PC 12 cells (Renneisen *et al.*, J Biol Chem. 1990 Sep 25;265(27):16337-42; Muller *et al.*, DNA Cell Biol. 1990 Apr;9(3):221-9). In addition, 25 liposomes are free of the DNA length constraints that are typical of viral-based delivery systems. Liposomes have been used effectively to introduce genes, various drugs, radiotherapeutic agents, enzymes, viruses, transcription factors, allosteric effectors and the like, into a variety of cultured cell lines and animals. Furthermore, the use of liposomes does not appear to be associated with autoimmune responses or unacceptable 30 toxicity after systemic delivery.

In certain embodiments, liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs).

Alternatively, in other embodiments, the invention provides for pharmaceutically-acceptable nanocapsule formulations of the compositions of the present invention. Nanocapsules can generally entrap compounds in a stable and reproducible way (see, for example, Quintanar-Guerrero *et al.*, Drug Dev Ind Pharm. 1998 Dec;24(12):1113-28). To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1 μm) may be designed using polymers able to be degraded *in vivo*. Such particles can be made as described, for example, by Couvreur *et al.*, Crit Rev Ther Drug Carrier Syst. 1988;5(1):1-20; zur Muhlen *et al.*, Eur J Pharm Biopharm. 1998 Mar;45(2):149-55; Zambaux *et al.* J Controlled Release. 1998 Jan 2;50(1-3):31-40; and U. S. Patent 5,145,684.

Cancer Therapeutic Methods

Immunologic approaches to cancer therapy are based on the recognition that cancer cells can often evade the body's defenses against aberrant or foreign cells and molecules, and that these defenses might be therapeutically stimulated to regain the lost ground, e.g. pgs. 623-648 in Klein, Immunology (Wiley-Interscience, New York, 1982). Numerous recent observations that various immune effectors can directly or indirectly inhibit growth of tumors has led to renewed interest in this approach to cancer therapy, e.g. Jager, *et al.*, Oncology 2001;60(1):1-7; Renner, *et al.*, Ann Hematol 2000 Dec;79(12):651-9.

Four basic cell types whose function has been associated with antitumor cell immunity and the elimination of tumor cells from the body are: i) B-lymphocytes which secrete immunoglobulins into the blood plasma for identifying and labeling the nonself invader cells; ii) monocytes which secrete the complement proteins that are responsible for lysing and processing the immunoglobulin-coated target invader cells; iii) natural killer lymphocytes having two mechanisms for the destruction of tumor cells, antibody-dependent cellular cytotoxicity and natural killing; and iv) T-lymphocytes possessing antigen-specific receptors and having the capacity to recognize

a tumor cell carrying complementary marker molecules (Schreiber, H., 1989, in Fundamental Immunology (ed). W. E. Paul, pp. 923-955).

Cancer immunotherapy generally focuses on inducing humoral immune responses, cellular immune responses, or both. Moreover, it is well established that 5 induction of CD4⁺ T helper cells is necessary in order to secondarily induce either antibodies or cytotoxic CD8⁺ T cells. Polypeptide antigens that are selective or ideally specific for cancer cells, particularly pancreatic cancer cells, offer a powerful approach for inducing immune responses against pancreatic cancer, and are an important aspect of the present invention.

10 In further aspects of the present invention, the pharmaceutical compositions described herein may be used for the treatment of cancer, particularly for the immunotherapy of pancreatic cancer. Within such methods, the pharmaceutical compositions described herein are administered to a patient, typically a warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer.
15 Accordingly, the above pharmaceutical compositions may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs. As discussed above, administration of the
20 pharmaceutical compositions may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous 25 host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established 30 tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host

immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and 5 macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive 10 immunotherapy.

Monoclonal antibodies may be labeled with any of a variety of labels for desired selective usages in detection, diagnostic assays or therapeutic applications (as described in U.S. Patent Nos. 6,090,365; 6,015,542; 5,843,398; 5,595,721; and 4,708,930, hereby incorporated by reference in their entirety as if each was incorporated 15 individually). In each case, the binding of the labelled monoclonal antibody to the determinant site of the antigen will signal detection or delivery of a particular therapeutic agent to the antigenic determinant on the non-normal cell. A further object of this invention is to provide the specific monoclonal antibody suitably labelled for achieving such desired selective usages thereof.

Effector cells may generally be obtained in sufficient quantities for 20 adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of 25 cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides 30 or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a

polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive 5 long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced 10 into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitory, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical 15 compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for 20 individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor 25 cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose 30 ranges from about 25 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

10 Cancer Detection and Diagnostic Compositions, Methods and Kits

In general, a cancer may be detected in a patient based on the presence of one or more pancreatic tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as pancreatic cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a pancreatic tumor sequence should be present at a level that is at least two-fold, preferably three-fold, and more preferably five-fold or higher in tumor tissue than in normal tissue of the same type from which the tumor arose. Expression levels of a particular tumor sequence in tissue types different from that in which the tumor arose are irrelevant in certain diagnostic embodiments since the presence of tumor cells can be confirmed by observation of predetermined tissue differential expression levels, e.g., 2-fold, 5-fold, etc, in tumor tissue to expression levels in normal tissue of the same type.

Other differential expression patterns can be utilized advantageously for diagnostic purposes. For example, in one aspect of the invention, overexpression of a tumor sequence in tumor tissue and normal tissue of the same type, but not in other

normal tissue types, e.g. PBMCs, can be exploited diagnostically. In this case, the presence of metastatic tumor cells, for example in a sample taken from the circulation or some other tissue site different from that in which the tumor arose, can be identified and/or confirmed by detecting expression of the tumor sequence in the sample, for 5 example using RT-PCR analysis. In many instances, it will be desired to enrich for tumor cells in the sample of interest, e.g., PBMCs, using cell capture or other like techniques.

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., 10 Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

15 In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a 20 binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to 25 which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full length pancreatic tumor proteins and polypeptide portions thereof to which the binding agent binds, as described above.

30 The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support

may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. 5 Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and 10 functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In 15 general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally 20 be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding 25 partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized 30 on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody

complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

5 More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20TM (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to
10 bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with pancreatic cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least
15 about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

20 Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20TM. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

 The detection reagent is then incubated with the immobilized antibody-
25 polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter
30 group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent

groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of 5 the reaction products.

To determine the presence or absence of a cancer, such as pancreatic cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is 10 the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical 15 Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the 20 value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off 25 value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, 30 labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of

bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent.

5 Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the

10 biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about

15 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to

20 those of ordinary skill in the art that the above protocols may be readily modified to use tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of

25 T cells that specifically react with a tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4 $^{+}$ and/or CD8 $^{+}$ T cells isolated from a patient is incubated with a tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected.

30 Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by

Ficoll/Hyapque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is 5 preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on 10 the level of mRNA encoding a tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the tumor protein. The amplified cDNA is 15 then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers 20 and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a tumor protein of the invention that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a 25 polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule 30 having a sequence as disclosed herein. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold*

Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another aspect of the present invention, cell capture technologies may be used in conjunction, with, for example, real-time PCR to provide a more sensitive tool for detection of metastatic cells expressing pancreatic tumor antigens. Detection of pancreatic cancer cells in biological samples, e.g., bone marrow samples, peripheral blood, and small needle aspiration samples is desirable for diagnosis and prognosis in pancreatic cancer patients.

Immunomagnetic beads coated with specific monoclonal antibodies to surface cell markers, or tetrameric antibody complexes, may be used to first enrich or positively select cancer cells in a sample. Various commercially available kits may be used, including Dynabeads® Epithelial Enrich (Dynal Biotech, Oslo, Norway), StemSep™ (StemCell Technologies, Inc., Vancouver, BC), and RosetteSep (StemCell Technologies). A skilled artisan will recognize that other methodologies and kits may also be used to enrich or positively select desired cell populations. Dynabeads® Epithelial Enrich contains magnetic beads coated with mAbs specific for two glycoprotein membrane antigens expressed on normal and neoplastic epithelial tissues. The coated beads may be added to a sample and the sample then applied to a magnet, thereby capturing the cells bound to the beads. The unwanted cells are washed away and the magnetically isolated cells eluted from the beads and used in further analyses.

RosetteSep can be used to enrich cells directly from a blood sample and consists of a cocktail of tetrameric antibodies that targets a variety of unwanted cells and crosslinks them to glycophorin A on red blood cells (RBC) present in the sample, forming rosettes. When centrifuged over Ficoll, targeted cells pellet along with the free RBC. The combination of antibodies in the depletion cocktail determines which cells will be removed and consequently which cells will be recovered. Antibodies that are available include, but are not limited to: CD2, CD3, CD4, CD5, CD8, CD10, CD11b, CD14, CD15, CD16, CD19, CD20, CD24, CD25, CD29, CD33, CD34, CD36, CD38, CD41, CD45, CD45RA, CD45RO, CD56, CD66B, CD66e, HLA-DR, IgE, and 10 TCR $\alpha\beta$.

Additionally, it is contemplated in the present invention that mAbs specific for pancreatic tumor antigens can be generated and used in a similar manner. For example, mAbs that bind to tumor-specific cell surface antigens may be conjugated to magnetic beads, or formulated in a tetrameric antibody complex, and used to enrich 15 or positively select metastatic %% tumor cells from a sample. Once a sample is enriched or positively selected, cells may be lysed and RNA isolated. RNA may then be subjected to RT-PCR analysis using %% tumor-specific primers in a real-time PCR assay as described herein. One skilled in the art will recognize that enriched or selected populations of cells may be analyzed by other methods (*e.g.* *in situ* hybridization or 20 flow cytometry).

In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays 25 may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

30 Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound

binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple tumor protein markers 5 may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided 10 herein may be combined with assays for other known tumor antigens.

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may 15 contain a monoclonal antibody or fragment thereof that specifically binds to a tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct 20 or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a tumor protein. Such an oligonucleotide may be used, for 25 example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a tumor protein.

SEQ ID NOs of the instant application claim priority according to the following:
30

Application 60/265,305 filed January 30, 2001	SEQ ID NOs:1-74	566P1
Application 60/305,484 filed July 12, 2001	SEQ ID NOs:75-453	566P2

	Application 60/333,626 filed November 27, 2001	SEQ ID NOS:454-455	566P3
	Application 60/267,568 filed February 9, 2001	SEQ ID NOS:456-528	570P1
	Application 60/265,682 filed January 31, 2001	SEQ ID NOS:529-4272	567P1
	Application 60/278,651 filed March 21, 2001	SEQ ID NOS:4273-4345	567P2
5	Application 60/287,121 filed April 27, 2001	SEQ ID NOS:4346-4546	567P3
	Application 60/313,999 filed August 20, 2001	SEQ ID NOS:4547-4554	567P5

The following Examples are offered by way of illustration and not by way of limitation.

10

EXAMPLES

EXAMPLE 1

15

IDENTIFICATION OF PANCREATIC TUMOR PROTEIN CDNAS FROM A PCR-BASED SUBTRACTION LIBRARY.

This Example discloses the isolation and identification of cDNA molecules from a cDNA library enriched in polynucleotides encoding secreted and transmembrane proteins.

20 25 30

A cDNA library was constructed by the method of Kopczynski *et al.* from mRNA purified from rough endoplasmic reticulum (RER) isolated from primary pancreatic tumor cells (PANC 391-34). *Proc. Natl. Acad. Sci.* 95:9973-9978 (1998) (incorporated herein by reference in its entirety). Briefly, cDNA was prepared from isolated mRNA by employing standard methodology. See, e.g., Ausubel *et al.*, "Short Protocols in Molecular Biology" (4th ed., 1999). The resulting cDNAs were ligated into a LAMBDA ZAP EXPRESS™ vector (Stratagene; La Jolla, California) and mass excision was then employed to generate a plasmid library in *E. coli*. Individual *E. coli* colonies were isolated and the cDNA clones subjected to nucleic acid sequencing. The nucleotide sequences of exemplary clones are disclosed herein as SEQ ID NOS:1-66, 75-152, 174-177, 182, 184-452, 454-4550. The predicted amino acid sequences of these clones are presented as SEQ ID NOS:67-74, 153-173, 178-181, 183, 453, 4551-4554 and 4558-4560.

A cDNA library was also constructed and cloned into the PCR2.1 vector (Invitrogen, Carlsbad, CA) by subtracting a pool of one or more tumor cDNAs with a pool of cDNA from normal tissues, for example, colon, spleen, brain, liver, kidney, lung, stomach and small intestine, using PCR subtraction methodologies (Clontech, 5 Palo Alto, CA). The subtraction is performed using a PCR-based protocol, which is modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA are separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, Sall and StuI). This digestion results in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from 10 digestion with RsaI according to the Clontech protocol. This modification does not affect the subtraction efficiency. Two tester populations are then created with different adapters, and the driver library remains without adapters.

The tester and driver libraries are then hybridized using excess driver cDNA. In the first hybridization step, driver is separately hybridized with each of the 15 tester cDNA populations. This results in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs, and (d) unhybridized driver cDNAs. The two separate hybridization reactions are then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) 20 through (d), a fifth population (e) is generated in which tester cDNA with one adapter is hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step results in enrichment of differentially expressed sequences which can be used as templates for PCR amplification with adapter-specific primers. The ends are then filled in, and PCR amplification is performed using adapter-specific primers. Only 25 population (e), which contained tester cDNA that do not hybridize to driver cDNA, are amplified exponentially. A second PCR amplification step is then performed, to reduce background and further enrich differentially expressed sequences. This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are over-expressed in pancreatic tumor tissue may be recoverable. Such transcripts 30 would be difficult to recover by traditional subtraction methods.

EXAMPLE 2ANALYSIS OF cDNA EXPRESSION OF PANCREATIC TUMOR cDNAs USING
MICROARRAY TECHNOLOGY

5 To determine mRNA expression levels of the isolated cDNA clones, cDNA clones from the pancreatic tumor subtraction library were randomly picked and colony PCR amplified. Their mRNA expression levels in pancreatic tumor, normal pancreas and various other normal tissues were determined using microarray technology (Rosetta Inpharmatics, Inc., Kirkland, WA). Briefly, the PCR amplification 10 products were arrayed onto slides into an array format, with each product occupying a unique location in the array. To do this, mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. Data was analyzed using software provided by 15 the manufacturer.

In additional studies, sequences disclosed herein were evaluated for overexpression in specific tumor tissues by microarray analysis. Using this approach, clones from the cDNA library described in Example 1 were randomly picked, PCR amplified, and their mRNA expression profiles in tumor and normal tissues were 20 examined using cDNA microarray technology essentially as described (Shena, M. *et al.*, 1995 Science 270:467-70). In brief, the clones were arrayed onto glass slides as multiple replicas, with each location corresponding to a unique cDNA clone (as many as 5500 clones can be arrayed on a single slide, or chip). Each chip was hybridized with a pair of cDNA probes that were fluorescence-labeled with Cy3 and Cy5, 25 respectively. Typically, 1 µg of polyA⁺ RNA was used to generate each cDNA probe. After hybridization, the chips were scanned and the fluorescence intensity recorded for both Cy3 and Cy5 channels. There were multiple built-in quality control steps. First, the probe quality was monitored using a panel of ubiquitously expressed genes. Secondly, the control plate also included yeast DNA fragments of which 30 complementary RNA may be spiked into the probe synthesis for measuring the quality of the probe and the sensitivity of the analysis. Currently, the technology offers a

sensitivity of 1 in 100,000 copies of mRNA. Finally, the reproducibility of this technology was ensured by including duplicated control cDNA elements at different locations.

Those cDNAs showing at least two-fold overexpression in tumor samples as compared to normal samples, and/or demonstrating overexpression based on visual analysis of the microarray data, were searched against Genbank and the results are shown in Table 2. These sequences are set forth in SEQ ID NOS:75-129. Full-length cDNA and protein sequences for 28 of these clones are disclosed in SEQ ID NOS:130-183 and are shown in Table 3.

10

TABLE 2

Microarray and Genbank Search Results for Pancreas cDNAs

SEQ ID NO:	Element (384 384)	Well 384	Plate:well 96	Pancrease Chip 2 Microarray Data				Blastn
				Clone ID	Ratio	Median Signal 1	Median Signal 2	
75	PCX352_ r01c15	a 15	838:A8	80150	2.37	0.648	0.273	Hu. p53-induced protein PIGPC1, transmembrane protein (THW gene)
76	PCX352_ r01c16	a 16	838:B8	80151	1.88	0.292	0.156	Hu. serine (or cysteine) proteinase inhibitor, clade E
77	PCX352_ r01c23	a 23	838:A12	80152	1.83	0.906	0.496	Hu. keratin 18 (KRT18)
78	PCX352_ r03c11	c 11	838:E6	80153	1.06	0.481	0.456	Hu. Rab geranylgeranyltransferase, beta subunit (RABGFTB)
79	PCX352_ r04c03	d 3	838:G2	80154	1.06	0.193	0.183	Hu. FAT tumor suppressor (Drosophila) homolog (FAT)
80	PCX352_ r04c11	d 11	838:G6	80155	1.55	0.999	0.645	Hu. mRNA for transmembrane protein (THW gene), p53- induced protein PIGPC1 (PIGPC1)
81	PCX352_ r07c03	g 3	839:E2	80156	0.95	0.253	0.266	Hu. fibrillarin (FBL)

SEQ ID NO:	Element (384)	Well 384	Plate:well 96	Pancrease Chip 2 Microarray Data				Blastn
				Clone ID	Ratio	Median Signal 1	Median Signal 2	
82	PCX352_r08c06	h 6	839:H3	80157	0.76	0.273	0.359	Hu. fibrillarin (FBL)
83	PCX352_r10c16	j 16	840:D8	80158	2.75	0.937	0.34	Hu. p53-induced protein PIGPC1, transmembrane protein (THW gene)
84	PCX352_r10c24	j 24	840:D12	80159	5.14	3.94	0.767	Hu. similar to collagen, type I, alpha 1; Collagen I, alpha-1 polypeptide
85	PCX352_r12c04	l 4	840:H2	80161	1.89	0.51	0.27	Hu. serine (or cysteine) proteinase inhibitor, clade E
86	PCX352_r12c07	l 7	840:G4	80162	0.77	0.314	0.407	Hu. pM5 protein (PM5)
87	PCX352_r12c20	l 20	840:H10	80163	1.55	0.72	0.466	Hu. fibrillarin (FBL)
88	PCX352_r15c03	o 3	841:E2	80164	1.5	0.178	0.119	Hu. type I transmembrane receptor (seizure-related protein)(PSK-1)
89	PCX352_r15c17	o 17	841:E9	80165	2.14	1.219	0.568	Hu. CD24 antigen (small cell lung carcinoma cluster 4antigen) (CD24)
90	PCX352_r16c08	p 8	841:H4	80166	0.59	0.192	0.329	Hu. fibrillarin (FBL)
91	PCX353_r01c03	a 3	842:A2	80167	2.68	0.071	0.027	Hu. highly similar to glucose-6-phosphate dehydrogenase; ubiquitin-like protein (GdX)
92	PCX353_r02c11	b 11	842:C6	80168	2.87	1.156	0.403	Hu. p53-induced protein PIGPC1, transmembrane protein (THW gene)
93	PCX353_r02c23	b 23	842:C12	80169	2.72	1.001	0.368	Hu. p53-induced protein PIGPC1, transmembrane protein (THW gene)
94	PCX353_r06c08	f 8	843:D4	80170	1.84	1.602	0.87	Hu. keratin 18 (KRT18)

SEQ ID NO:	Element (384	Well 384	Plate:well 96	Pancrease Chip 2 Microarray Data				Blastn
				Clone ID	Ratio	Median Signal 1	Median Signal 2	
95	PCX353_r07c22	g 22	843:F11	80171	1.6	0.588	0.368	Hu. plastin 3 (T isoform) (PLS3)
96	PCX353_r08c06	h 6	843:H3	80173	1.55	0.378	0.244	Hu. liver-specific bHLH-Zip transcription factor (LISCH7)
97	PCX353_r13c20	m 20	845:B10	80175	1.22	0.26	0.214	Hu. collagen, type XVIII, alpha 1 (COL18A1)
98	PCX353_r13c23	m 23	845:A12	80176	1.59	0.432	0.272	Hu. tissue factor pathway inhibitor 2 (TFPI2), placental protein 5 (PP5)
99	PCX353_r16c10	p 10	845:H5	80178	1.72	1.116	0.649	Hu. tumor antigen (L6)
100	PCX354_r01c03	a 3	846:A2	80180	1.57	0.095	0.06	Hu. small EDRK-rich factor 1B (centromeric) (SERF1B)
101	PCX354_r03c02	c 2	846:F1	80181	1.8	0.951	0.53	Hu. p53-induced protein PIGPC1, transmembrane protein (THW gene)
102	PCX354_r04c04	d 4	846:H2	80183	1.17	0.301	0.258	Hu. fibrillarin (FBL)
103	PCX354_r04c10	d 10	846:H5	80184	1.76	0.545	0.31	Hu. BAC clone RP11-549B18 from 18
104	PCX354_r05c14	e 14	847:B7	80185	2	1.475	0.739	Hu. tumor antigen (L6)
105	PCX354_r05c21	e 21	847:A11	80186	3.6	1.049	0.291	Novel (short/ poor sequence)
106	PCX354_r08c03	h 3	847:G2	80187	3.03	0.335	0.11	Hu. thrombospondin 2 (THBS2)
107	PCX354_r08c14	h 14	847:H7	80188	1.58	1.032	0.654	Hu. clone RP11-527G2, DKFZP564A2416 protein
108	PCX354_r08c23	h 23	847:G12	80189	2.38	1.421	0.596	Hu. tumor antigen (L6)
109	PCX354_r09c15	i 15	848:A8	80191	2.44	0.602	0.247	Hu. p53-induced protein PIGPC1, transmembrane protein (THW gene)

SEQ ID NO:	Element (384)	Pancrease Chip 2 Microarray Data						Blastn
		Well 384	Plate:well 96	Clone ID	Ratio	Median Signal 1	Median Signal 2	
110	PCX354_r09c19	i 19	848:A10	80192	2.22	0.753	0.339	Hu. p53-induced protein PIGPC1, transmembrane protein (THW gene)
111	PCX354_r11c13	k 13	848:E7	80193	2	0.391	0.196	Hu. sema domain, immunoglobulin domain (Ig), short basicdomain, secreted, (semaphorin) 3C (SEMA3C)
112	PCX354_r11c19	k 19	848:E10	80194	2.2	1.718	0.783	Hu. connective tissue growth factor (CTGF)
113	PCX354_r12c15	l 15	848:G8	80195	2.15	1.144	0.533	Hu. p53-induced protein PIGPC1, transmembrane protein (THW gene)
114	PCX355_r01c03	a 3	850:A2	80196	1.79	0.092	0.051	Human mitochondrion
115	PCX355_r02c11	b 11	850:C6	80197	1.96	1.442	0.735	Hu. connective tissue growth factor (CTGF)
116	PCX355_r07c23	g 23	851:E12	80198	1.91	1.295	0.679	Hu. keratin 18 (KRT18)
117	PCX355_r10c23	j 23	852:C12	80199	1.68	0.823	0.489	Hu. keratin 18 (KRT18)
118	PCX353_r08c01	h 1	843:G1	80172	1.65	0.482	0.291	Hu. serine (or cysteine) proteinase inhibitor, clade E
119	PCX353_r10c11	j 11	844:C6	80174	1.45	0.412	0.285	Hu. FAT tumor suppressor (Drosophila) homolog (FAT)
120	PCX353_r15c02	o 2	845:F1	80177	1.05	0.47	0.446	Hu. similar to heterochromatin-like protein 1
121	PCX353_r16c16	p 16	845:H8	80179	1.76	1.259	0.715	Hu. transmembrane protein (THW gene), PIGPC1
122	PCX354_r09c03	i 3	848:A2	80190	2.35	0.789	0.336	Hu. p53-induced protein PIGPC1, transmembrane protein (THW g

SEQ ID NO:	Element (384	Well 384	Plate:well 96	Pancrease Chip 2 Microarray Data				Blastn
				Clone ID	Ratio	Median Signal 1	Median Signal 2	
123	PCX355_r11c11	k 11	852:E6	80200	1.9	0.881	0.463	Hu. tumor antigen (L6)
124	PCX355_r15c13	o 13	853:E7	80201	1.67	0.414	0.248	Hu. stearoyl-CoA desaturase (SCD)
125	PCX356_r03c06	c 6	854:F3	80203	1.58	0.59	0.373	Hu. chromogranin B (secretogranin 1)
126	PCX356_r04c20	d 20	854:H10	80204	3.1	0.062	0.02	Hu. serine (or cysteine) proteinase inhibitor, clade E
127	PCX356_r06c11	f 11	855:C6	80205	2.01	1.117	0.556	Hu. tumor antigen (L6), transmembrane 4 superfamily member 1
128	PCX356_r07c24	g 24	855:F12	80207	1.69	0.301	0.178	Novel - short sequence
129	PCX356_r12c21	l 21	856:G11	80208	1.5	0.254	0.169	Hu. Fer-1 (<i>C. elegans</i>)-like 3 (myoferlin)

TABLE 3

Full-length cDNA and Protein sequences for Pancreas cDNAs

SEQ ID NO: (Full-Length cDNA/Pro)	Clone Name	Clone ID	GenBank Identity/Sequence from BLASTN of SeqID
130/153	IodesPanChip2-1	80150	Hu.p53-induced protein PICPCL, transmembrane protein (THW gene)
131/154	IodesPanChip2-2	80151	Hu.serine (or cysteine) proteinase inhibitor, clade E
132/155	IodesPanChip2-3	81052	Hu.keratin 18 (KRT18)
133/156	IodesPanChip2-4	81053	Hu.Rab geranylgeranyltransferase, beta subunit (RABGGTB)
134/157	IodesPanChip2-5	81054	Hu.FAT tumor suppressor (Drosophila) homolog (FAT)
135/158	IodesPanChip2-7	80156	Hu.fibrillarin (FBL)
136/159	IodesPanChip2-10	80159	Hu.similar to collagen, type I, alpha 1; Collagen I, alpha-1 polypeptide
137/160	IodesPanChip2-13	80162	Hu.pM5 protein (PM5)
138/161	IodesPanChip2-15	80164	Hu.type I transmembrane receptor (seizure-related protein) (PSK-1)
139/162	IodesPanChip2-16	80165	Hu.CD24 antigen (small cell lung carcinoma cluster 4 antigen) (CD24)
140	IodesPanChip2-18	80167	Hu.highly similar to glucose-6-phosphate dehydrogenase
141/163		80167	Hu.ubiquitin-like protein (GdX)
142/164	IodesPanChip2-22	80171	Hu.plastin 3 (T isoform) (PLS3)
143/165	IodesPanChip2-24	80173	Hu.liver-specific bHLH-Zip transcription factor (LISCH7)
144/166	IodesPanChip2-26	80175	Hu.collagen, type XVIII, alpha 1 (COL18A1)

SEQ ID NO: (Full Length cDNA/Pro)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SEQID
145/167	IodesPanChip2-27	80176	Hu. tissue factor pathway inhibitor 2 (TFPI2), placental protein 5 (PP5)
146/168	IodesPanChip2-29	80178	Hu. tumor antigen (L6)
147/169	IodesPanChip2-31	80180	(SERF1A)
148/170	IodesPanChip2-31	80180	Hu.small EDRK-rich factor 1B (centromeric) (SERF1B)
149/171	IodesPanChip2-38	80187	Hu.thrombospondin 2 (THBS2)
150/172	IodesPanChip2-44	80193	Hu.sema domain, immunoglobulin domain (Ig), short basidomain, secreted, (semaphorin) 3C (SEMA3C)
151/173	IodesPanChip2-45	80194	Hu.connective tissue growth factor (CTGF)
152	IodesPanChip2-47	80196	Human pHL-1 gene, c-myc oncogene containing coxIII sequence
174/178	IodesPanChip2-28	80177	Heterochromatin-like protein 1
175/179	IodesPanChip2-52	80201	Hu. steroyl-CoA desaturase (SCD)
176/180	IodesPanChip2-54	80203	Hu. chromogranin B (secretogranin 1)
177/181	IodesPanChip2-59	80208	Hu. Fer-1 (C.elegans)-like 3 (myoferlin)
182/183	IodesPanChip2-11	80160	Hu. clone MGC:15409; 93% homology to NF-IL6

EXAMPLE 3IDENTIFICATION OF ADDITIONAL PANCREATIC TUMOR PROTEIN CDNAS
FROM AN EXPRESSION LIBRARY

5 The PCR-based subtraction library described in Example 1 was further screened to isolate additional cDNAs expressed in pancreatic tumor cells. An additional 268 clones were identified and are disclosed in SEQ ID NOS:184-452. The clones were sequenced and the sequences used in a BLAST search against Genbank. Those sequences showing some degree of similarity to sequences in Genbank are
 10 described in Table 4. Those sequences showing no significant similarity to sequences in Genbank are listed in Table 5.

TABLE 4

Pancreas Tumor Sequences Showing Some Degree of Similarity to Sequences in
Genbank

SEQ ID NO: (Full-Length cDNA)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SEQID
185	PNCM-2	71232	Hu. putative ionotropic glutamate receptor GLURR2
186	PNCM-3	71233	Hu. accessory proteins BAP31/BAP29, 6C6-Ag, CDM
188	PNCM-5	71235	Hu. prosaposin (PSAP), sphingolipid activator protein 1
189	PNCM-6	71236	Hu.similar to adaptor-related protein complex 3, sigma 2subunit Hu.alanyl (membrane) aminopeptidase (aminopeptidase N)
190	PNCM-7	71237	Hu.prosaposin
191	PNCM-8	73408	Hu. ribosome binding protein 1, ES130
192	PNCM-9	73409	Hu. kinecin 1 (kinesin receptor) (KTN1)
193	PNCM-11	73410	Hu. Protein A kinase (PPKA) anchor protein (gravin) 12
194	PNCM-12	71238	Hu.golgi autoantigen, golgin subfamily a, 4 (GOLGA4)
195	PNCM-13	73411	Hu. kinecin 1 (kinesin receptor) (KTN1)

SEQ ID NO: (Full-Length cDNA)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SEQID
196	PNCM-14	71239	Hu.prosaposin
197, 198	PNCM-15	73412	Hu.prosaposin
199	PNCM-16	71240	Hu.prosaposin
200	PNCM-18	71241	Hu.prosaposin
201	PNCM-19	71242	Hu.centrromere protein F (350/400kD, mitosin) (CENPF)
202	PNCM-20	73413	Hu. lamin A/C (nuclear env. protein)
203	PNCM-21	71243	Hu.prosaposin
204	PNCM-22	71244	Hu.prosaposin
205	PNCM-23	71245	Hu.methyl-CpG binding domain protein 2 (MBD2)
206	PNCM-24	71246	Hu.prosaposin
207	PNCM-25	71247	Hu.prosaposin
208	PNCM-26	71248	Hu.prosaposin
209	PNCM-27	71249	Hu. E3 ubiquitin ligase SMURF2
210	PNCM-28	73414	Hu.Kinectin 1
211	PNCM-29	71250	Hu.fer-1 (<i>C.elegans</i>)-like 3 (myoferlin) (FERIL3)
214	PNCM-32	71253	Hu.ECSIT (Toll/IL-1 signal transduction)
215	PNCM-33	71254	Hu. villin 2, cytovillin 2, (ezrin) (VIL2)
216, 217	PNCM-34	71255	Hu.mitotic checkpoint protein isoform MAD1a (MAD1)
218	PNCM-35	71256	Hu.Homer-2A
219	PNCM-36	73415	Macaca fascicularis brain cDNA, clone:QfLA- 11332
220	PNCM-37	71257	Hu. prosaposin
221	PNCM-38	71258	Hu.methyl-CpG binding domain protein 2 (MBD2)
222	PNCM-39a	71259	Hu. lamin A/C (nuclear env. protein)
223	PNCM-39b	73416	Hu. sphingolipid activator proteins 1 and 2 processed/mutant
224	PNCM-40	71260	Hu. rabaptin-5 (RABSEP) (endocytic transport)
225	PNCM-41	73376	Hu.fer-1
226	PNCM-42	73377	Hu.CD36 antigen-like 2, lysosomal

SEQ ID NO: (Full-Length cDNA)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SeqID
sialoglycoprotein			
227	PNCM-43	73378	Hu. Protein A kinase (PPKA) anchor protein (gravin) 12
228	PNCM-44	73379	Hu. Prosaposin
229, 230	PNCM-47	73381	Hu. mitochondrion
231	PNCM-48	73382	Hu.vimentin (VIM)
232, 233	PNCM-49	73383	Hu.hydroxysteroid (17-beta) dehydrogenase 4
234, 235	PNCM-50	73384	Hu.amyloid beta (A4) precursor-like protein 2 (APL2)
236	PNCM-51	73385	Hu.Ran binding protein 2
237	PNCM-53	73386	Hu.alanyl (membrane) aminopeptidase (aminopeptidase N)
238	PNCM-56	73387	Hu. kinecin 1 (kinesin receptor) (KTN1)
239, 240	PNCM-57	73388	Hu. kinecin 1(Reverse orientation)
241, 242	PNCM-58	73389	Hu.vimentin (VIM)
243	PNCM-59	73390	Hu. glutathione-S-transferase like; glutahionetransferase omega
244	PNCM-60	73391	Hu. ribosome binding protein 1, ES/130, KIAA 1398
245	PNCM-61	73417	Hu.Ran binding protein 2
246	PNCM-62	73392	Hu. putative ionotropic glutamate receptor GLURR2
247	PNCM-63	73393	Hu.fer-1 (<i>C.elegans</i>)-like 3 (myoferlin) (FER1L3)
248	PNCM-65	73418	Hu. transferrin receptor (p90, CD71) (TFRC)
249	PNCM-66	73395	Hu. ribosome binding protein 1, ES/130, KIAA 1398
250	PNCM-67	73396	Hu.Similar to glucose regulated protein, 58kDa, cloneMGC:3178
251	PNCM-68	73397	Hu. kinecin 1 (kinesin receptor) (KTN1)
252, 253	PNCM-69	73419	Hu.cDNA FLJ10480 fis, clone NT2RP2000126
254	PNCM-70	73398	Hu. kinecin 1 (kinesin receptor) (KTN1)
255,256	PNCM-71	73399	Hu.TATA element modulatory factor 1 (TMF1)
257	PNCM-72	73400	Hu. enoyl Coenzyme A hydratase 1, peroxisomal (ECH1)

SEQ ID NO: (Full-Length cDNA)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SEQID
258, 259	PNCM-73	73420	Hu.prosaposin
260	PNCM-74	73401	Hu.vimentin (VIM) [bp]
261	PNCM-77	73404	Hu.prosaposin
262	PNCM-78	73405	Hu.golgi autoantigen, golgin subfamily a, 4 (GOLGA4)
263, 264	PNCM-80	73407	Hu. kinecin 1 (kinesin receptor) (KTN1)
265	PNCM-81	72174	Hu.ribosomal protein L9
266	PNCM-82	72175	Hu.putative transmembrane protein
267	PNCM-83	72176	Hu. kinecin 1 (kinesin receptor) (KTN1)
268	PNCM-84	72177	Hu.prosaposin
269	PNCM-85	72178	Hu. ORF (LOC51035) w/CpGisland and Ubiq.- binding domains
270	PNCM-86	72179	Hu. Protein A kinase (PRKA) anchor protein (gravin) 12 (AKAP12)
271, 272	PNCM-87	73421	Hu. heat shock 105kD, antigen NY-CO-25
273	PNCM-88	72180	Hu. heat shock 105kD, antigen NY-CO- 25(Colon cancer Ag.)
274	PNCM-89	72181	Hu. ferritin, heavy polypeptide 1 (FTH1)
275	PNCM-90	72182	Hu.frizzled (Drosophila) homolog 6 (FZD6)
276	PNCM-91	72183	Hu.vimentin (VIM)
277	PNCM-92	72184	Hu.Ran binding protein 2 [bp198-610], sperm membrane protein BS-63, nucleoporin (NUP358)
278	PNCM-93	72185	Hu. kinecin 1 (kinesin receptor) (KTN1)
279	PNCM-94	72186	Hu.Tax-1 (T-cell leukemia virus type I) bindingprotein 1 (TAX1BP1) [bp 923-1335]; TRAF6-binding protein T6BP (IL-1 signaling)
280	PNCM-95	72187	Hu. kinecin 1 (kinesin receptor) (KTN1) [bp 813-1223]
281	PNCM-96	72188	Hu.prosaposin [bp 608-1018]
282	PNCM-97	72189	Hu.heat shock 105kD...[bp 1-412]
283	PNCM-98	72190	Hu. clone IMAGE:3449323
284	PNCM-99	72191	Hu. rabaptin-5 [bp1578-1990]
285	PNCM-100	72192	Hu.TNF receptor-1 associated protein (TRADD)

SEQ ID NO: (Full-Length cDNA)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SEQID
286	PNCM-101	72193	Hu.trans-Golgi network protein
287	PNCM-102	72194	Hu.IMAGE:3355762, chromodomain helicase DNA binding protein 1-like
288	PNCM-103	72195	Hu. ribosome binding protein 1, ES/130 [bp1563-1975], KIAA1398
289	PNCM-106	72196	Hu.ubiquinol-cytochrome c reductase core protein II (UQCRC2)
290	PNCM-110	72197	Hu. ribosome binding protein 1, ES/130 [bp717-1129], KIAA1398
291	PNCM-112	72198	Hu.accessory proteins BAP31/BAP29 [bp237-648], 6C6-Ag, CDM
292	PNCM-113	72199	Hu.M-phase phosphoprotein 1 (MPHOSPH1)
293	PNCM-114	72200	Hu. serine palmitoyltransferase, subunit I (enzyme in sphingolipid biosynth.)
294	PNCM-115	72201	Hu. kinecin 1 (kinesin receptor) (KTN1)[bp 1896-2306]
295	PNCM-116	72202	Hu.Tax-1 [bp 1-380]
296	PNCM-117	72203	Hu. methyl-CpG binding domain protein 2 (MDB2)
297	PNCM-118	72204	Hu. cDNA: FLJ23027 fis, clone LNG01826
298	PNCM-119	72205	Hu. cDNA DKFZp586F1918
299, 300	PNCM-120	72206	Macaca fascicularis brain cDNA, clone QfIA-11332
301	PNCM-122	73422	Hu.heat shock 105kD, antigen NY-CO-25
302	PNCM-123	73423	Hu.IMAGE:3355762, chromodomain helicase DNA binding protein 1-like
303	PNCM-124	73424	Hu. kinecin 1 (kinesin receptor) KTN1) [bp]
304, 305	PNCM-125	73425	Hu.vimentin (VIM) [bp]
306	PNCM-126	74597	Hu.prosaposin
307, 308	PNCM-128	73426	Hu. cleavage stimulation factor, subunit 3, 77kD(CSTF3)
309, 310	PNCM-129	73427	Hu.diazepam binding inhibitor (GABA receptor modulator, acyl-Coenzyme A binding protein)
311	PNCM-131	73428	Hu.prosaposin
312	PNCM-132	73429	Hu., Similar to glucose regulated protein, 58kDa, cloneMGC:3178

SEQ ID NO: (Full-Length cDNA)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SEQID
313, 314	PNCM-133	74598	Hu. kinecin 1 (kinesin receptor) (KTN1)
315	PNCM-134	74599	Hu.prosaposin
316	PNCM-135	73430	Hu.,Similar to glucose regulated protein, 58 kDa, cloneMGC:3178
317, 318	PNCM-136	74600	Hu. ferritin, heavy polypeptide 1 (FTH1)
319, 320	PNCM-137	74601	Hu.accessory proteins BAP31/BAP29,6C6-Ag,CDM
321, 322	PNCM-138	73437	Hu. RER1 protein (RER1)
323, 324	PNCM-139	73438	Hu.prosaposin
325, 326	PNCM-141	73439	Hu.Tax-1(T-cell leukemia virus type I) bindingprotein (TAX1BP1)
327, 328	PNCM-142	73440	Hu. Protein A kinase (PRKA) anchor protein (gravin) 12
329	PNCM-143	73441	Hu.prosaposin
330, 331	PNCM-144	73442	Hu.prosaposin
332, 333	PNCM-145	73443	Hu.,Similar to glucose regulated protein, 58 kDa, cloneMGC:3178
336	PNCM-147	74602	Hu.fer-1 (<i>C.elegans</i>)-like 3 (myoferlin) (FER1L3)
337	PNCM-148	73445	Hu.prosaposin (PSAP),sphingolipid activator protein 1
338	PNCM-150	73456	Hu.heat shock 105kD,antigen NY-CO-25
339	PNCM-151	73585	Hu. heat shock 105kD (HSP-105B)
340, 341	PNCM-152	73586	Hu. Protein A kinase (PRKA) anchor protein (gravin) 12
342, 343	PNCM-153	73587	Hu. cleavage stimulation factor,subunit 3, 77kD(CSTF3)
344, 345	PNCM-154	73457	Hu.methyl-CpG binding domain protein 2 (MBD2)
346, 347	PNCM-155	74603	Hu. Protein A kinase (PRKA) anchor protein (gravin) 12
348	PNCM-157	73458	Hu. Protein A kinase (PRKA) anchor protein (gravin) 12
349, 350	PNCM-158	73459	Hu.low density lipoprotein-related protein- associated protein 1
351, 352	PNCM-159	73460	Hu.prosaposin

SEQ ID NO: (Full-Length cDNA)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SeqID
353	PNCM-160	73461	Hu.accessory proteins BAP31/BAP29 [bp155-662],6C6-Ag,CDM
354, 355	PNCM-161	74604	Hu. cleavage stimulation factor,subunit 3, 77kD(CSTF3)
356, 357	PNCM-162	74605	Hu.prosaposin, Hu.Tax-1
358, 359	PNCM-163	74606	Hu.leucine zipper-EF-hand containing transmembrane protein 1 (LETM1)
360, 361	PNCM-164	74607	Hu.CD36 antigen-like 2, lysosomal sialoglycoprotein
362, 363	PNCM-165	74608	Hu.prosaposin
364	PNCM-167	74610	Hu.transmembrane protein (63kD)
365	PNCM-169	74611	Hu.IMAGE:3355762,FLJ22530 fis, clone HRC12866,Hu.prosaposin, Hu.Tax-1
366, 367	PNCM-171	74613	Hu.leucine rich repeat (in FLII) interacting protein 1(LRRFIP1)
368, 369	PNCM-172	74614	Hu.prosaposin
370, 371	PNCM-173	74640	Hu.prosaposin
372, 373	PNCM-174	74615	Hu.,Similar to glucose regulated protein, 58 kDa, cloneMGC:3178
374, 375	PNCM-175	74616	Hu.,Similar to glucose regulated protein, 58 kDa, cloneMGC:3178
376	PNCM-176	74617	Hu.prosaposin
377	PNCM-177	77101	Hu. cleavage stimulation factor,subunit 3, 77kD(CSTF3)
378	PNCM-178	77102	Hu. Protein Protein A kinase (PRKA) anchor protein (gravin) 12
379	PNCM-180	77104	Hu.prosaposin
380, 381	PNCM-182	74618	Hu.prosaposin
382	PNCM-183	74619	Hu.Ran binding protein 2, sperm membrane protein BS-63, nucleoporin
383, 384	PNCM-185	74620	Hu.prosaposin
385, 386	PNCM-186	74621	Hu. ribosome binding protein 1,KIAA1398,clone RP11-462D18(5-prime)
387, 388	PNCM-188	74623	Hu.IMAGE:3355762,FLJ22530 fis, clone HRC12866
389, 390	PNCM-189	74624	Hu. Similar to glucose regulated protein, 58 kDa

SEQ ID NO: (Full-Length cDNA)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SEQID
			cloneMGC:3178
391, 392	PNCM-190	74625	Hu.Ran binding protein 2, sperm membrane protein BS-63, nucleoporin
393	PNCM-191	74631	Hu.diazepam binding inhibitor (GABA receptor modulator),acyl-Coenzyme A binding protein)
394, 395	PNCM-193	74632	Hu. endozepine, vimentin
396	PNCM-202	77105	Hu. glucose-regulated protein, 58kD (GRP58)
397	PNCM-208	77108	Hu. rabaptin-5 (RAB5EP)
398	PNCM-210	77109	Hu.vimentin (VIM)
399	PNCM-215	77114	Hu. hypothetical protein FLJ10634, clone MGC:944
400	PNCM-219	77118	Hu.alanyl (membrane) aminopeptidase (aminopeptidase N)
401	PNCM-221	77120	Hu.similar to RAN binding protein 2 [bp 576...],nucleoporin (NUP358), sperm-binding protein
402	PNCM-223	77122	Hu. cell surface glycoprotein/ cell adhesion molecule CD44
403	PNCM-224	77123	Hu.sperm membrane protein BS-63, RANBP2
404	PNCM-226	77125	Hu. Protein Protein A kinase (PRKA) anchor protein (gravin) 12
405	PNCM-229	77127	Prosaposin
406	PNCM-231	77129	Hu. Vimentin
407	PNCM-232	77130	Prosaposin
408	PNCM-234	77132	Prosaposin
409	PNCM-237	77134	Hu. Vimentin
410	PNCM-238	77135	Hu.accessory proteins BAP31/BAP29,6C6-Ag,CDM
411	PNCM-239	77136	Hu. ribosomal protein P0
412	PNCM-243	77139	Hu. rabaptin-5 (RAB5EP)
413	PNCM-244	77140	Prosaposin
414	PNCM-245	77141	Hu.,Similar to glucose regulated protein, 58 kDa, cloneMGC:3178
415	PNCM-248	77144	Hu. ORF (LOC51035);Similar to ORF, clone MGC:2274; clone MGC:5321

SEQ ID NO: (Full-Length cDNA)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SEQID
416	PNCM-250	77146	Hu.accessory proteins BAP31/BAP29[bp404],6C6-Ag,CDM
417	PNCM-253	77149	Hu. methyl-CpG binding domain protein 2 (MBD2)
418	PNCM-258	77474	Hu. Sim.to glucose-reg.protein[bp1-99];60bp: cGMP-specific phosphodiesterase
419	PNCM-266	77153	Hu.fer-1 (C.elegans)-like 3 (myoferlin) (FER1L3)
420	PNCM-267	77479	Hu. Kinectin 1
421	PNCM-268	77154	Hu.accessory proteins BAP31/BAP29,6C6- Ag,CDM
422	PNCM-269	77155	Hu. Kinectin 1
423	PNCM-271	77157	Hu. Kinectin 1
424	PNCM-272	77480	Hu.accessory proteins BAP31/BAP29,6C6- Ag,CDM
425	PNCM-278	77485	Prosaposin
426	PNCM-282	77487	Hu.methyl-CpG binding domain protein 2 (MBD2),antigen NY-CO-41
427	PNCM-283	77488	Hu. Kinectin 1
428	PNCM-287	77490	Hu. Kinectin 1
429	PNCM-293	77494	Hu. ribosome binding protein 1, ES/130
430	PNCM-294	77495	Hu. leucine zipper-EF-hand containing transmembraneprotein 1 (LETM1)
431	PNCM-298	77499	Hu. ribosome binding protein 1, ES/130
432	PNCM-300	77500	Prosaposin
433	PNCM-310	77160	Hu. uveal autoantigen
434	PNCM-311	77504	Hu.accessory proteins BAP31/BAP29,6C6- Ag,CDM
435	PNCM-314	77506	Prosaposin
436	PNCM-316	77507	Hu. Protein Protein A kinase (PRKA) anchor protein (gravin) 12
437	PNCM-318	77508	Prosaposin
438	PNCM-320	77509	Hu. ribosome binding protein 1, ES/130
439	PNCM-321	77162	Hu.uveal autoantigen
440	PNCM-322	77163	Hu.chromodomain helicase DNA binding protein

SEQ ID NO: (Full-Length cDNA)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SEQID
1-like(CHD1L)			
441	PNCM-324	77165	Hu.accessory proteins BAP31/BAP29,6C6-Ag.CDM
442	PNCM-326	77167	Hu.eukaryotic translation initiation factor 2, subunit 2(beta, 38kD) (EIF2S2)
443	PNCM-329	77169	Hu.veal autoantigen
444	PNCM-331	77171	Hu. Prosaposin
445	PNCM-332	77172	Hu.alanyl (membrane) aminopeptidase (aminopeptidase N)
446	PNCM-333	77173	Hu. Prosaposin
447	PNCM-337	77175	Hu.,Similar to glucose regulated protein, 58kDa, cloneMGC:3178
448	PNCM-338	77176	Hu. M-phase phosphoprotein 1
449	PNCM-341	77178	Hu. cDNA DKFZp586F1918
450	PNCM-345	77180	Hu.accessory proteins BAP31/BAP29,6C6-Ag.CDM
451	PNCM-348	77510	Prosaposin

TABLE 5

Pancreas Tumor Sequences Showing no Significant Similarity to Sequences in Genbank

SEQ ID NO: (Full-Length cDNA/Pro)	CLONE NAME	CLONE ID	GENBANK IDENTITY/SEQUENCE FROM BLASTN OF SEQID
184	PNCM-1	71231	
187	PNCM-4	71234	No match to bp376 - 50bp@92% w/prosaposin - 100bp no matchl
212	PNCM-30	71251	
213	PNCM-31	71252	
334, 335	PNCM-146	73444	

EXAMPLE 4

FULL-LENGTH SEQUENCE AND EXPRESSION ANALYSIS OF THE PN80E
PANCREATIC TUMOR PROTEIN CDNA

The full-length sequence of the cDNA clone 80186, (partial sequence 5 disclosed in SEQ ID NO:105), was determined and is disclosed in SEQ ID NO:454. This sequence was used to search against public databases and the results are described in Table 6.

TABLE 6

10 Database Search Results for clone 80186, pancreatic tumor candidate Pn80E

SEQ ID NO (Partial/Full- length):	Clone ID	Candidate Name	GenBank Blastn Results
105/454	80186	Pn80E	89% <i>Mus musculus</i> 18 days embryo cDNA, RIKEN full-length enriched library, clone:1110014B07-a secreted protein, with a C1q domain

The mRNA expression profile was then further analyzed by real-time PCR. The first-strand cDNA used in the quantitative real-time PCR was synthesized from 20 µg of total RNA that was treated with DNase 1 (Amplification Grade, Gibco 15 BRL Life Technology, Gaithersburg, MD) using Superscript Reverse Transcriptase (RT) (Gibco BRL Life Technology, Gaithersburg, MD). Real-time PCR was performed with a GeneAmp™ 5700 sequence detection system (PE Biosystems, Foster City, CA). The 5700 system uses SYBR™ green, a fluorescent dye that only intercalates into double stranded DNA, and a set of gene-specific forward and reverse primers. The 20 increase in fluorescence was monitored during the whole amplification process. The optimal concentration of primers was determined using a checkerboard approach and a pool of cDNAs from breast tumors was used in this process. The PCR reaction was performed in 25 µl volumes that included 2.5 µl of SYBR™ green buffer, 2 µl of cDNA template and 2.5 µl each of the forward and reverse primers for the gene of interest. The 25 cDNAs used for RT reactions were diluted 1:10 for each gene of interest and 1:100

for the β -actin control. In order to quantitate the amount of specific cDNA (and hence initial mRNA) in the sample, a standard curve was generated for each run using the plasmid DNA containing the gene of interest. Standard curves were generated using the Ct values determined in the real-time PCR which were related to the initial cDNA concentration used in the assay. Standard dilution ranging from $20-2 \times 10^6$ copies of the gene of interest was used for this purpose. In addition, a standard curve was generated for β -actin ranging from 200 fg-2000 fg. This enabled standardization of the initial RNA content of a tissue sample to the amount of β -actin for comparison purposes. The mean copy number for each group of tissues tested was normalized to a constant amount of β -actin, allowing the evaluation of the over-expression levels seen with each of the genes.

Real-time PCR analysis as described above showed that Pn80E is over-expressed in a panel of pancreatic tumors, including metastatic tumors. Pn80E is also expressed in normal pancreas tissue, adrenal gland, aorta, skin and trachea. Low levels of expression were observed in bone, brain, bronchus, colon, esophagus, heart, kidney, liver, lung, pituitary, skeletal muscle, spinal cord, and spleen. These differential expression patterns indicate that this antigen may be used for immunotherapeutic purposes and/or as a diagnostic marker in individuals with pancreatic cancer.

20

EXAMPLE 5

FULL-LENGTH SEQUENCE AND EXPRESSION ANALYSIS OF THE PN81E PANCREATIC TUMOR PROTEIN CDNA

The full-length sequence of the cDNA clone 80207, (partial sequence disclosed in SEQ ID NO:128), was determined and is disclosed in SEQ ID NO:455. No matches were identified when this sequence was used to search against public databases.

The mRNA expression profile of Pn81E was then analyzed by real-time PCR as described in Example 4. This analysis showed that Pn81E is over-expressed in a panel of pancreatic tumors and normal pancreas samples as compared to a panel of 30 normal tissues including bone marrow, esophagus, gall bladder, heart, kidney, lung, skeletal muscle, small intestine, and stomach. Expression was observed in bone,

PBMC, and spleen. Lower levels of expression were observed in brain, bronchus, colon, liver, pituitary gland, skin, spinal chord, and trachea. These results indicate that the Pn81E antigen may be used in diagnostic and immunotherapy applications.

EXAMPLE 6

5 PREPARATION OF A PCR-BASED cDNA SUBTRACTION LIBRARY FROM
PANCREATIC TUMORS

A cDNA subtraction library containing cDNA from primary pancreatic tumors subtracted with cDNA from normal tissues (liver, salivary gland, small intestine, stomach, heart, brain, bone marrow and normal lung) was constructed as follows. Total 10 RNA was extracted from primary tissues using Trizol reagent (Gibco BRL Life Technologies, Gaithersburg, MD) as described by the manufacturer. The polyA+ RNA was purified using an oligo(dT) cellulose column according to standard protocols. First strand cDNA was synthesized using the primer supplied in a Clontech PCR-Select cDNA Subtraction Kit (Clontech, Palo Alto, CA). The driver DNA consisted of cDNAs 15 from normal tissues with the tester cDNA being from two primary pancreatic tumors. Double-stranded cDNA was synthesized for both tester and driver, and digested with a combination of endonucleases (MluI, MscI, PvuII, Sall and StuI) which recognize six-nucleotide restriction sites. This modification of the digestion procedure resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from 20 digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. The digested tester cDNAs were ligated to two different adaptors and the subtraction was performed according to Clontech's protocol.

The tester and driver libraries were then hybridized using excess driver 25 cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to 30 populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the

second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that 5 did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that r are transcripts that are overexpressed in pancreatic tumor 10 tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

The resulting PCR products were subcloned into the TA cloning vector, pCRII (Invitrogen, San Diego, CA) and transformed into ElectroMax *E. coli* DH10B cells (Gibco BRL Life, Technologies) by electroporation. DNA was isolated from 15 independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division (Foster City, CA) Automated Sequencer Model 373A.

Seventy three randomly selected cDNA clones in the subtracted pancreatic tumor-specific cDNA library were characterized by DNA sequencing and by subsequent Genbank and EST Blast database searches. Sequences of these partial 20 cDNAs are provided in SEQ ID NO:456-528.

Three thousand seven hundred forty four randomly selected cDNA clones in the subtracted pancreatic tumor-specific cDNA library were characterized by DNA sequencing and by subsequent Genbank and EST Blast database searches. Sequences of these partial cDNAs are provided in SEQ ID NO:529-4346.

25

EXAMPLE 7

MICROARRAY AND SEQUENCE ANALYSIS OF CDNA CLONES OVEREXPRESSED IN PANCREAS TUMORS

30 One hundred thirty-eight individual clones analyzed using microarray technology as described in Example 2 showed between 3 to 4.5-fold overexpression in

pancreas tumors as compared to normal tissues. These cDNA clones were sequenced using standard protocols and compared to public databases (SEQ ID NO:4347-4484). Those cDNAs that showed some degree of similarity to sequences in the databases are described in Table 7. Those cDNAs showing no significant similarity to known 5 sequences in the database are described in Table 8.

Pancreas Tumor cDNA Clones Showing Some Degree of Similarity to Sequences in Genbank

TABLE 7

SEQ ID NO:	Element (384)	Element (96)	Ratio	Median Signal 1	Median Signal 2	Genset	Contig	Genbank
4346	p0150r10c11	R0580 C6	4.18	0.341	0.082	61	1	Secretogranin II (Chromogranin C)
4347	p0150r07c17	R0579 E9	3.68	0.163	0.044	42	1	Secretogranin II (Chromogranin C)
4348	p0150r09c15	R0580 A8	3.63	0.236	0.065	53	1	Secretogranin II (Chromogranin C)
4349	p0150r07c14	R0579 F7	3.01	0.214	0.071	46	1	Secretogranin II (Chromogranin C)
4350	p0150r11c05	R0580 E3	4.38	0.096	0.022	66	1	Secretogranin II (Chromogranin C)
4351	p0160r06c18	R0619 D9	3.43	0.266	0.077	134	2	Pancreatic Lipase
4352	p0160r02c21	R0618 C11	3.6	0.202	0.056	133	2	Pancreatic Lipase
4353	p0160r13c02	R0621 B1	3.24	0.202	0.062	135	2	Pancreatic Lipase
4354	p0150r13c04	R0581 B2	3.66	0.188	0.051	84	3	Secretogranin II (Chromogranin C)
4355	p0150r02c15	R0578 C8	4.45	0.131	0.029	11	3	ATP binding cassette, subfamily B, (MDR 1)
4356	p0150r06c12	R0579 D6	3.02	0.274	0.091	39	4	Human gene for JKTBP1, JKTBP1
4357	p0151r08c12	R0583 D6	3.4	0.112	0.033	104	5	26S proteasome regulatory subunit
4358	P0150r14c04	R0581 D2	3.17	0.161	0.051	87	6	Chromosome 5 CTC-487M23
4359	p0150r02c06	R0578 D3	3.28	0.193	0.059	14	7	cDNA clone FLJ21238 lis, clone COLO1115
4360	p0150r04c19	R0578 G10	3.91	0.192	0.049	23	8	GTP cyclotidolase 1
4361	p0150r03c18	R0578 F9	3.94	0.153	0.041	22	9	Clone RP1-353C18 on chromosome 20
4362	p0151r13c03	R0585 A2	3.51	0.249	0.071	108	10	Spectrin SH3 domain binding protein 1
4363	p0150r01c08	R0578 B4	3.86	0.171	0.044	5	11	Human decay accelerating factor (CD55) gene
4364	p0150r11c07	R0580 E4	3.02	0.143	0.048	67	12	BAC clone GS1-66B6 7/p15.2-p13
4365	P0150r02c11	R0578 C6	3.33	0.148	0.045	10	13	RNA (guanine-7-methyltransferase
4366	p0150r01c17	R0578 A9	4.14	0.202	0.049	2	14	Clone RP1-15c14 on chromosome 6q15-16.3
4367	p0150r05c16	R0579 B8	3.63	0.131	0.036	32	15	Human sarcoendoplasmic reticulum protein
4368	p0150r06c04	R0579 D2	3.82	0.315	0.083	36	16	Clone 2013 on chromosome Xq25-26
4369	p0150r15c17	R0581 E9	3.18	0.104	0.033	92	17	Clone 2013 on chromosome Xq25-26

SEQ ID NO:	Element (384)	Element (96)	Ratio	Median Signal 1	Median Signal 2	Genset	Contig	Genbank
4370	p0150r15c11	R0581 EG	3.47	0.147	0.043	91	18	Human cytoplasmic dynein intermediate chain isoform IC-2
4371	p0150r09c13	R0580 A7	3.9	0.143	0.037	52	19	Human aldehyde dehydrogenase 1
4372	p0150r13c03	R0581 A2	3.14	0.222	0.071	80	20	cDNA DKFZp43C2112
4373	p0150r09c10	R0580 B5	3.03	0.226	0.075	57	21	Human RAD21 homolog
4374	p0161r13c17	R0525 A9	3.39	0.217	0.064	136	22	Pancreatic carboxypapillidase B1
4375	p0150r16c21	R0617 G11	4.1	0.2	0.049	132	23	Human matrix metalloproteinase 2
4377	p0150r09c19	R0584 A10	3.31	0.139	0.042	106	25	Clone RP1-315G1 on chromosome Xq24-25
4378	p0151r02c06	R0582 D3	3.46	0.326	0.094	101	26	cDNA FLJ20882 is clone ADKv03206
4379	p0150r16c06	R0581 H3	3.37	0.155	0.046	100	27	Human potassium channel modulatory factor
4380	p0150r09c12	R0580 B6	4	0.111	0.028	58	28	Human protein convertase subtilisin/kexin type 2
4381	p0150r07c06	R0579 F3	3.37	0.195	0.058	43	29	KIAA0205 gene
4382	p0150r09c19	R0579 C10	3.34	0.178	0.053	34	30	Human Rhamnitolate synthase
4383	p0150r04c05	R0578 G3	3.72	0.218	0.059	24	31	Clone RP1-179B15
4384	p0150r03c21	R0578 E11	4.17	0.2	0.048	18	32	KIAA0970 protein
4385	p0150r15c07	R0581 E4	3.83	0.102	0.027	90	33	Human myosin X
4386	p0150r02c18	R0578 D9	4.46	0.143	0.032	16	33	Human myosin X
4387	p0150r01c15	R0580 C8	4.46	0.247	0.056	62	34	KIAA1390 protein
4388	p0150r07c05	R0579 E3	3.12	0.135	0.043	40	35	cDNA DKFZp686E2023
4389	p0150r06c08	R0579 D4	3.85	0.177	0.046	37	36	Human hypothetical protein FLJ10134
4390	p0150r01c24	R0578 B12	3.74	0.18	0.048	4	37	Human ALEX1 protein
4391	p0150r07c15	R0579 E8	3.13	0.272	0.087	41	38	Human tropomodulin
4392	p0150r02c23	R0578 C12	4.34	0.163	0.037	8	39	Human Krasle maf-related leucine zipper homolog
4393	p0150r09c08	R0584 B4	4.44	0.393	0.089	107	40	Human histone acetyltransferase
4394	p0150r16c09	R0581 G5	3.55	0.238	0.067	95	41	Human coronin, actin-binding protein 1C
4395	p0150r14c11	R0581 C6	3.99	0.096	0.024	86	42	cDNA DKFZp761(G2423
4396	p0151r05c12	R0583 B6	3.49	0.221	0.063	103	43	Human X-prolyl aminopeptidase-like

SEQ ID NO:	Element (384)	Element (96)	Ratio	Median Signal 1	Median Signal 2	Genset	Contig	Genbank
4397	R0580_G12	4.06	0.14	0.034	0.034	75	44	Clone RP-756N20 on chromosome 1p31.3-32
4398	p0150r1f6c02	R0581_H1	3.09	0.093	0.03	98	45	KIAA1228 protein
4399	p0155r1f0c08	R0600_D4	3.07	0.245	0.08	121	46	cDNA DKF7265881_1419
4400	p0150r0d2c05	R0578_C3	3.82	0.174	0.046	9	47	Human uncharacterized hypothalamus protein HARP11
4401	p0150r0f9c04	R0580_B2	3.09	0.197	0.064	55	48	Human aldehyde dehydrogenase 1
4402	p0150r0f3c22	R0578_F11	3.45	0.133	0.039	21	49	Human secretory granule, neuroendocrine protein 1
4403	p0150r1f5c10	R0581_F5	3.1	0.111	0.036	94	50	Human L-Beta-1,3-N-acetylgalactosaminyltransferase
4404	p0150r1f3c20	R0581_B10	3.94	0.111	0.028	82	51	Human 12p13.3 BAC RPC111-356L7
4405	p0150r0f8c18	R0579_H9	3.36	0.173	0.052	49	52	Human tumor differentially expressed 1
4406	p0150r0f9c22	R0580_B11	3.39	0.195	0.057	54	53	Human deoxyribonuclease kinase
4408	p0163r0f4c09	R0650_G5	3	0.283	0.094	138	55	Human hypothetical protein FLJ10540
4409	p0155r0f1c04	R0580_B2	4.2	0.377	0.09	116	56	Human collagen, type III, alpha 1
4410	p0152r1f6c22	R0589_H11	3.74	0.363	0.097	113	57	Human transmembrane 4 superfamily member 4 (TM4SF4)
4411	p0152r1f6c12	R0589_H6	3.09	0.292	0.095	114	58	Human chloride intracellular channel 1
4413	p0150r0f5c23	R0579_A12	4.1	0.189	0.046	27	60	Human N33 protein form 2
4414	p0150r1f1c09	R0580_E5	3.16	0.191	0.06	68	61	Human hypothetical protein (FLJ11127)
4415	p0150r1f3c22	R0581_B11	3.1	0.12	0.039	83	62	DNA sequence from clone 422623 on chromosome 6q24
4416	p0150r1f1c17	R0580_E9	3.66	0.244	0.067	70	63	cDNA FLJ20935 fs, clone ADSE01534
4417	p0159r1f6c01	R0617_G1	4.4	0.183	0.042	131	64	Human carboxypeptidase A2
4418	p0158r1f6c21	R0605_G11	3.37	0.206	0.061	122	65	Human guanine nucleotide exchange factor
4419	p0150r0f8c15	R0579_C8	3.21	0.168	0.052	35	66	Human chromosome 5 clone CTC-315Q24
4422	p0150r1f1c22	R0580_F11	4.29	0.17	0.04	72	69	Human RNA helicase II/Gu protein gene
4425	p0150r1f6d2	R0580_F1	3.65	0.207	0.057	71	72	Human carboxypeptidase E
4426	p0157r0f7c21	R0607_E11	3.88	0.192	0.049	126	73	Human cutaneous T-cell lymphoma tumor antigen set07-2

SEQ ID NO:	Element (384)	Element (96)	Ratio	Median Signal 1	Median Signal 2	Genset	Contig	Genbank
4427	p0150r16c17	R0581 G9	3.28	0.101	0.031	97	74	KIAA0353 protein
4428	p0155r03c08	R0588 F4	3.25	0.305	0.094	117	75	Human laminin gamma 2
4429	p0150r07c10	R0579 F5	3.27	0.223	0.068	44	76	Human chromosome 5 clone CTC-576H9
4430	p0150r16c13	R0581 G7	3.58	0.166	0.046	96	77	Clone RP11-71J12 on chromosome 13
4431	p0150r06c10	R0579 D5	3.05	0.243	0.08	38	78	Human 3q25.2-27 BAC RPC11463J4
4432	p0150r02c16	R0578 DB	4.47	0.11	0.025	15	79	Human potassium inwardly-rectifying channel, subfamily J
4433	p0150r09c06	R0580 B3	4.25	0.176	0.042	56	80	KIAA1699 protein
4434	p0150r11c16	R0580 F8	3.49	0.178	0.051	74	81	Human somatostatin receptor 2
4435	p0150r01c13	R0578 A7	4.49	0.411	0.092	1	82	Human claudin-12
4436	p0150r08c10	R0579 H5	3.29	0.238	0.073	48	83	Human tumor rejection antigen (gp96), 1
4438	p0158r14c18	R0617 D9	3.07	0.101	0.033	130	85	Human carboxypeptidase A2
4439	p0150r16c22	R0581 H11	3.09	0.304	0.098	99	86	Human cDNA FLJ12280 (fs clone MAMMA10 107744
4440	p0152r10c20	R0588 D10	4.4	0.157	0.036	110	87	Human granine nucleotide-binding protein alpha-subunit
4441	p0150r13c23	R0581 A12	3.48	0.248	0.071	79	88	Human nuclear factor kappa-B DNA binding subunit
4442	p0150r12c10	R0580 H5	3.7	0.158	0.043	78	89	Human C0164 isoform delta 4
4443	p0150r09c18	R0580 B9	3.67	0.214	0.058	59	90	Human galectin-3 gene
4444	p0158r08c04	R0612 B2	4.14	0.14	0.034	129	91	Human cathepsin C
4445	p0150r08c09	R0579 G5	3.69	0.226	0.061	47	92	Human imidazoline receptor candidate
4446	p0150r11c11	R0580 E6	4.15	0.237	0.057	69	93	Human glutaminase isoform C
4447	p0150r15c01	R0581 E1	4.12	0.099	0.024	88	94	Human chromosome 5 clone CTD-2314G24
4448	p0151r70r00	R0607 E1	3.67	0.254	0.069	125	95	DNA from chromosome 19, cosmid F21056
4449	p0150r09c21	R0580 A11	3.49	0.169	0.048	51	96	Human false p73 target protein gene
4450	p0150r12c02	R0580 H1	3.31	0.173	0.052	76	97	cDNA FLJ12346 fs, clone NT2RP2005254
4451	p0150r03c17	R0578 E9	4.16	0.212	0.051	20	98	cDNA DKF7Zp4-34L1715
4453	p0150r05c20	R0579 B10	3.43	0.147	0.043	29	100	Human large conductance calcium-activated potassium channel beta

SEQ ID NO:	Element (384)	Element (96)	Ratio	Median Signal 1	Median Signal 2	Genset	Config	Genbank
4454 p0150n05c04	R0579 B2	3.01	0.1	0.033	31	101		Human prostate tumor over expressed gene 1
4455 p0150n07c12	R0579 F6	3.59	0.191	0.053	45	102		Human alpha-L-fucosidase gene
4456 p0150n05c02	R0579 B1	3.15	0.205	0.065	28	103		Human N-terminal acetyltransferase complex arcd1 subunit
4457 p0150r13c24	R0589 B12	3.44	0.207	0.06	111	104		Chromosome 19, cosmid F236S9
4458 p0150n03c11	R0578 E6	3.05	0.159	0.052	19	105		Human IK cytokine, down-regulator of HLA II
4459 p0162r13c11	R0529 A6	3.07	0.133	0.043	137	106		Human thrombospondin 2
4460 p0151r13c15	R0555 A8	3.71	0.171	0.046	109	107		cDNA FLJ23160 lis, clone LNGG0682
4461 p0150n03c01	R0578 E1	4.03	0.145	0.036	17	108		Human Na+/glucose cotransporter gene
4462 p0151r08c17	R0583 G9	3.57	0.131	0.037	105	109		Human death-associated protein
4463 p0150n01c02	R0578 B1	3.1	0.287	0.093	3	110		Human guanine nucleotide binding protein
4464 p0150r04c06	R0578 H3	3.93	0.158	0.04	25	111		Clone RP4-81B7 on chromosome 1
4465 p0150n09c19	R0580 A10	3.86	0.197	0.051	50	112		Human mitochondrial
4466 p0153r06c10	R0591 D5	3.78	0.294	0.078	115	113		Human DEAD/H box polypeptide 5
4467 p0150n02c20	R0578 D10	3.82	0.198	0.052	13	114		KIAA1317 protein
4468 p0155n06c08	R0560 B4	4.13	0.393	0.095	118	115		KIAA0853 protein
4471 p0150r13c02	R0561 B1	3.13	0.163	0.052	81	117		RNA binding motif protein 5
4473 p0150n16c3	R0580 E12	3.57	0.237	0.067	65	119		Human GTP cyclohydrolase 1
4474 p0155r10c24	R0580 D12	3.55	0.205	0.058	120	120		Human mitochondrial DNA control region
4475 p0157r06c03	R0607 C2	4.14	0.172	0.042	124	121		Ras-related C3 botulinum toxin substrate 1
4476 p0150n05c24	R0579 B12	3.83	0.157	0.041	30	122		Human hypothetical protein FLJ20391
4479 p0155r10c19	R0600 C10	3.73	0.274	0.073	119	125		KIAA0292 protein
4480 p0150r14c23	R0581 C12	3.51	0.14	0.04	85	126		ISL1 transcription factor, LM/homeodomain
4481 p0150r10c19	R0560 C10	3.56	0.188	0.053	60	127		KIAA0766 gene
4482 p0150r11c19	R0580 E10	3.28	0.152	0.046	63	128		KIAA1554 protein
4483 p0150r15c21	R0581 E11	3.25	0.114	0.035	89	129		Chromosome 1p14.3 PAC clone pDJ239b22
4484 p0150r11c21	R0580 E11	3.07	0.165	0.054	64	130		Clone RP1-309f20 on chromosome 20
4412 p0150n01c16	R0578 B8	3.06	0.242	0.079	7	59		Human thyroid hormone receptor coactivating protein

TABLE 8

Pancreas Tumor cDNAs Showing no Significant Similarity to Known

Sequences in Genbank

SEQ ID NO:	Element (384)	Element (96)	Ratio	Median Signal 1	Median Signal 2	Genset	Contig
4376	p0150r02c02	R0578 D1	3.62	0.193	0.053	12	24
4407	p0157r08c09	R0607 G5	3.18	0.155	0.049	128	54
4420	p0151r05c04	R0583 B2	3.01	0.145	0.048	102	67
4421	p0150r05c21	R0579 A11	3.4	0.217	0.064	26	68
4423	p0150r01c14	R0578 B7	3.67	0.19	0.052	6	70
4424	p0150r15c08	R0581 F4	3.06	0.111	0.036	93	71
4437	p0150r05c18	R0579 B9	3.98	0.164	0.041	33	84
4452	p0157r07c20	R0607 F10	3.09	0.158	0.051	127	99
4469	p0152r16c01	R0589 G1	3.13	0.242	0.077	112	116
4471	p0150r12c22	R0580 H11	4	0.15	0.037	77	118
4476	p0150r11c04	R0580 F2	4.03	0.175	0.043	73	123
4477	p0156r16c18	R0605 H9	3.03	0.201	0.066	123	124

5

EXAMPLE 8MICROARRAY AND SEQUENCE ANALYSIS OF ADDITIONAL CDNA CLONES
OVEREXPRESSED IN PANCREAS TUMORS

- Forty eight hundred clones from three PCR-based subtracted cDNA libraries were PCR amplified and arrayed on DNA chips. They were hybridized with fluorescently labeled probes which were generated from pancreatic tumors and a variety of normal tissues including normal pancreas. The array data were analyzed by computer and by visual analysis. Sixty-three clones with 4.5-fold overexpression in pancreatic tumors were selected and their sequences were determined by DNA sequencing (SEQ ID NO:4485-4547). The sequences were then searched against public databases including Genbank and EST. Those cDNAs that showed some degree of similarity to sequences in the databases are described in Table 9. Those cDNAs showing no significant similarity to known sequences in the database are described in Table 10. Several of these cDNAs have been selected as promising candidates for therapeutic and diagnostic purposes. The candidate names are also shown in Tables 9 and 10.

TABLE 9

Additional Pancreas Tumor cDNA Clones Showing Some Degree of Similarity to Sequences in the Genbank							
SEQ ID NO:	Element (384) Element (96) Ratio	Median Signal 1	Median Signal 2	Contig	Identity	Candidate	
4533	p01570/c23	R0607 E12	15.8	0.097	0.006	BAC clone CTA-271G13 from 7	
4518	p01570/c17	R0607 A9	16.38	0.168	0.01	cDNA FLJ12849 fts, clone NT2RP2003393	
4506	p01500/09c01	R0580 A1	9.73	0.106	0.011	cDNA FLJ21368 fts, clone COL03056	
4519	p01570/c13	R0607 E7	46.35	0.12	0.003	cDNA FLJ21410 fts, clone COL03938	
4521	p01570/c15	R0607 E5	12.34	0.137	0.011	cDNA FLJ23867 fts, clone ING16050	Pn1474P
4507	p01500/08c17	R0579 G9	5.2	0.137	0.026	Chromogranin B	Pn1468P
4514	p01501/c208	R0580 H4	7.88	0.046	0.006	Chromosome 12 clone 91705	
4524	p01520/08c10	R0587 D5	11.83	0.038	0.003	Chromosome 5 clone CTC-53442	
4509	p01500/09c20	R0580 B10	6.1	0.131	0.021	Chromosome 5 clone CTD-2031P19	
4500	p01501/c01	R0580 E1	6.34	0.14	0.022	Chromosome 5 clone CTD-212K27	
4523	p01550/07c16	R0589 F8	4.7	0.107	0.023	Chromosome 7 clone RP11-24Bk17	
4487	p01570/c17	R0607 E9	8.97	0.148	0.017	Clone 27K12 on chromosome 6p11.2-12.3	
4539	p01570/c69	R0607 E5	5.64	0.262	0.046	Clone RP1-122P22 on chromosome 20	Pn1473P
4501	p01500/03c14	R0578 F7	9.86	0.138	0.014	Clone RP11-239L20 on chromosome 6	
4529	p01570/d5c18	R0607 B9	24.3	0.174	0.007	Discoidin domain receptor family, Human mammary carcinoma kinase	
4498	p01500/02c07	R0578 C4	4.99	0.264	0.053	DKFZp434M7616	
4508	p01500/09c17	R0580 A9	16.97	0.121	0.007	Guanine nucleotide binding protein (neuroendocrine secretory protein 55)	
4510	p01500/08c06	R0579 H3	5.32	0.113	0.021	Hormone-regulated Repro-PC 1.0 gene	
4537	p0151r12c17	R0584 G9	5.37	0.937	0.174	Reprogen Inc, KIAA1342	
4513	p01501/c03	R0580 E2	19.29	0.056	0.005	Human breast tumor protein immunogenic fragment	
						Human CG1-86 protein	

SEQ ID NO:	Element (3/4) Element (9/6) Ratio	Median Signal 1	Median Signal 2	Contig	Identity	Candidate
4546	p0156705c06	R0607 F3	16.6	0.18	0.011	Human clone RP722 unknown mRNA
4540	p0156705c05	R0607 G3	20.8	0.353	0.017	Human colon cancer nucleotide sequence, NCA
4526	p015002c03	R0578 C2	5.65	0.166	0.029	Human decidual protein induced by progesterone
4517	p0150r15c23	R0581 E12	7.72	0.143	0.019	Human Desmoplakin
4530	p015705c17	R0607 C9	8.13	0.222	0.027	Human flamin gene (FLNB)
4504	p015001c04	R0578 B2	10.45	0.095	0.009	Human foetal brain secreted protein
4534	p0150r1c20	R0578 B10	4.82	0.295	0.061	Human Hexosaminidase B beta-subunit
4496	p015007c01	R0579 E1	8.7	0.107	0.012	Human HLA gene for MHC class I antigen, B4701 allele MDM2 gene
4484	p015705c22	R0607 B11	8.32	0.211	0.025	Human long-chain fatty acid coenzyme A ligase
4488	p0150r15c22	R0581 F11	9.35	0.115	0.012	Human putative helicase RUVBL (LOC58897)
4511	p0150r13c19	R0581 A10	5.09	0.217	0.043	Human PVR gene
4503	p015004c17	R0578 G9	6.29	0.404	0.064	Human secreted protein gene 79
4582	p0150r11c14	R0580 F7	31.67	0.1	0.003	Human secretory granule, neuroendocrine protein 1
4485	p015705c21	R0607 A11	5.18	0.149	0.029	Human starch-isomaltase
4531	p015707c18	R0607 F9	38.09	0.183	0.005	Human transgelin
4544	p015202c05	R0626 C3	5.16	0.434	0.084	hXAG
4485	p015706c05	R0607 C3	9.62	0.128	0.013	KIAA0071
4527	p015008c24	R0578 D12	4.75	0.112	0.024	KIAA0804
4516	p0150r08c11	R0580 A6	5.32	0.227	0.043	KIAA286
4541	p015705c17	R0607 G9	5.58	0.213	0.038	Malate dehydrogenase 2, NAD
4495	p0150r05c19	R0578 A10	11.78	0.112	0.01	MMD2 gene
4536	p0150r15c06	R0581 F3	6.86	0.227	0.033	Neuroendocrine secretory protein 55
4489	p0159r03c13	R0614 E7	5.97	0.549	0.092	Pancreatic lipase
4490	p0160r04c18	R0518 H9	4.56	0.374	0.008	Proalpha 1(I) collagen
4545	p015705c24	R0607 D12	18.84	0.157	0.008	Pro alpha 1(I) collagen
4515	p0150r05c22	R0579 B11	4.63	0.187	0.04	PRO2000 protein

SEQ ID NO:	Element (394) Element (96)	Ratio	Median Signal 1	Median Signal 2	Contig	Protein identified by the signal sequence trap	Identity	Candidate
4520	p0157r07c14	R0607 F7	26.74	0.149	0.006	33	polyA site DNA	
4543	p0161r16c06	R0625 H3	5.96	1.13	0.19		Regenerating islet-derived 1 beta	
4491	p0150r08c23	R0579 C12	4.79	0.133	0.028	7	RP1-287F15 chromosome 9	
4492	p0150r02c15	R0578 C8	4.45	0.131	0.029	7	RP1-287F15 chromosome 9	
4493	p0150r15c24	R0581 B12	6.41	0.138	0.021	8	Secretogranin II	
4494	p0150r15c03	R0581 E2	6.13	0.126	0.021	8	Secretogranin II	
4502	p0150r02c12	R0578 D6	6.07	0.149	0.025	15	Secretogranin II	
4505	p0150r02c22	R0578 D11	5.65	0.147	0.026	18	Secretogranin II	

TABLE 10

Additional Pancreas Tumor cDNAs Showing no Significant Similarity

to Known Sequences in Genbank

SEQ ID NO:	Element (384)	Element (96)	Ratio	Median Signal 1	Median Signal 2	Contig	Candidate
4497	p0150r06c16	R0579 D8	4.93	0.105	0.021	10	
4499	p0152r15c23	R0589 E12	4.91	0.186	0.038	12	Pn1471P
4512	p0150r12c09	R0580 G5	4.6	0.083	0.018	25	
4522	p0151r01c08	R0582 B4	5.1	0.158	0.031	35	
4525	p0150r04c18	R0578 H9	5.3	0.145	0.027	38	
4532	p0157r06c08	R0607 D4	11.23	0.093	0.008	45	
4535	p0150r14c15	R0581 C8	5.19	0.102	0.02		Pn1470P
4538	p0155r12c15	R0600 G8	5.35	0.772	0.145		
4542	p0160r03c01	R0618 E1	4.73	0.489	0.104		Pn1476P

5

EXAMPLE 9QUANTITATIVE REAL-TIME PCR ANALYSIS OF cDNA CLONES
OVEREXPRESSED IN PANCREATIC TUMORS

Four pancreas clones selected by cDNA microarray and subtracted 10 cDNA library as described in Examples 2 and 6-8 were analyzed by real-time PCR to confirm their expression level in a variety of tissues. Pancreatic tumors and normal pancreas tissues along with other normal tissues were tested in quantitative real-time PCR. Briefly, the first-strand cDNA was synthesized from 20 μ g of total RNA that had been treated with DNase I (Amplification Grade, Gibco BRL Life Technology, 15 Gaithersburg, MD), using Superscript Reverse Transcriptase (RT) (Gibco BRL Life Technology, Gaithersburg, MD). Real-time PCR was performed with a GeneAmpTM 5700 sequence detection system (PE Biosystems, Foster City, CA). The 5700 system uses SYBRTM green, a fluorescent dye that only intercalates into double stranded DNA, and a set of gene-specific forward and reverse primers. The increase in fluorescence is 20 monitored during the whole amplification process. The optimal concentration of primers was determined using a checkerboard approach and a pool of cDNAs from pancreas tumors was used in this process. The PCR reaction was performed in 25 μ l volumes that include 2.5 μ l of SYBR green buffer, 2 μ l of cDNA template and 2.5 μ l each

of the forward and reverse primers for the gene of interest. The cDNAs used for RT reactions were diluted 1:10 for each gene of interest and 1:100 for the β -actin control. In order to quantitate the amount of specific cDNA (and hence initial mRNA) in the sample, a standard curve is generated for each run using the plasmid DNA containing 5 the gene of interest. Standard curves were generated using the Ct values determined in the real-time PCR which were related to the initial cDNA concentration used in the assay. Standard dilution ranging from $20-2 \times 10^6$ copies of the gene of interest was used for this purpose. In addition, a standard curve was generated for β -actin ranging from 200fg-2000fg. This enabled standardization of the initial RNA content of a tissue 10 sample to the amount of β -actin for comparison purposes. The mean copy number for each group of tissues tested was normalized to a constant amount of β -actin, allowing the evaluation of the over-expression levels seen with each of the genes.

Pn1467P (SEQ ID NO:4503) was found to be over-expressed in grade IV pancreas tumors and the majority of grade III tumors. Moderate expression was 15 observed in grade II tumors, normal pancreas, and in most normal tissues. Over-expression of Pn1470P (SEQ ID NO:4535) was seen in grade III tumors and normal pancreas. Moderate expression of this gene was observed in grade IV tumors. Over-expression was also seen in bronchus. Low to moderate expression was observed in gall bladder, PBMC, stomach testis, and thymus. Pn1475P (SEQ ID NO:4540) was 20 over-expressed in grades II-IV pancreas tumors and expressed at a low level in normal pancreas. Expression was not seen in metastatic tumors or in pancreatitis. Some Pn1475P expression was observed in bronchus, colon, esophagus, gall bladder, lung, salivary gland, small intestine, stomach, and trachea. Pn1476 (SEQ ID NO:4542) was overexpressed in 4 of 11 grade III tumors, 1 grade II, and 1 grade IV tumor. It was also 25 overexpressed in 3 of 4 normal pancreas samples. No expression of this gene was observed in any normal tissues. Thus, this candidate will be valuable for both vaccine and diagnostic purposes. Pn1468P (SEQ ID NO:4507) was over-expressed in pancreas tumor metastases but not in other pancreas tumors. Over-expression was also observed in adrenal gland and pituitary, but was absent from all other normal tissues. Pn1473P 30 (SEQ ID NO:4539) was highly over-expressed in pancreas tumor sample T795A. It was also over-expressed in 1 of 3 grade II pancreas tumor samples, 2 of 6 grade 4 tumor

samples, and 7 of 11 grade III tumor samples. It was also over-expressed in tumor metastases but was not expressed in normal pancreas tissue. Pn1473P expression was also observed in skeletal muscle, stomach, testis, and trachea. The expression profiles of all of these candidate genes suggest that they will be valuable for therapeutic vaccine
5 and/or diagnostic purposes.

EXAMPLE 10

FULL LENGTH CDNA AND PROTEIN SEQUENCE FOR 4 ANTIGENS OVEREXPRESSED IN PANCREATIC TUMORS

10

The sequences for Pn1468P, Pn1472P, and Pn1475P (SEQ ID NOs:4507, 4529, 4540, respectively), shown to be overexpressed in pancreas tumor samples, were searched against Genbank and the full length sequences identified. The full length sequences from Genbank are set forth in SEQ ID NOs:4548, 4549, and 4550, 15 respectively. The corresponding protein sequences are set forth in SEQ ID NOs:4552-4554. The sequence for Pn1467, also overexpressed in pancreas tumor samples, was searched against the Genseq database and the full length sequence identified. The full length cDNA sequence from Genseq is set forth in SEQ ID NO:4547 and the corresponding protein sequence is set forth in SEQ ID NO:4551.

20

EXAMPLE 11

FULL LENGTH CDNA AND PROTEIN SEQUENCE FOR 2 ANTIGENS OVEREXPRESSED IN PANCREATIC TUMORS

Disclosed herein are the full-length DNA and protein sequences for the Pn1509P and Pn1510P antigens, both overexpressed in pancreatic tumors as compared 25 to normal tissues.

A partial sequence for Pn1509P was shown to be overexpressed by 3.74 fold in pancreatic tumors as compared to normal tissues (see SEQ ID NO:4410, Table 2). The full-length DNA sequence for Pn1509P was identified by searching the 493 base pair fragment of Pn1509P set forth in SEQ ID NO:4410 against the Genbank 30 database. The full-length extended DNA sequence for Pn1509P (identified in GenBank

accession number NM 004617) is set forth in SEQ ID NO:4555 and the corresponding protein is set forth in SEQ ID NO:4558. Based on sequence analysis, Pn1509 is predicted to be a tetraspan protein (it has four predicted membrane spanning domains) and has two potential sites for N-linked glycosylation.

5 A partial sequence for Pn1510P was shown to be overexpressed by 3.03 fold in pancreatic tumors as compared to normal tissues (see SEQ ID NO:4477, Table 2). The partial Pn1510P sequence set forth in SEQ ID NO:4477 was used in a search of the GeneSeq DNA database and matched 5 GeneSeq DNA records: A26456, A37144, A26424, V84525, and T22133. When the 5 protein coding regions of these DNA
10 sequences were aligned using the DNASTar Seqman program, it was found that record A37144 had an additional C at position 35. This resulted in a 243 amino acid ORF. In the absence of this C at position 35, the DNA sequence encodes a 278 amino acid ORF. Disclosed herein are the DNA sequences that encode for both the 243 amino acid ORF and the 278 amino acid ORF (SEQ ID NOS:4556 and 4557, respectively). Also
15 disclosed herein are the protein sequences for the 243 (Pn1510P-243) and 278 (Pn1510P-278) amino acid ORFs (SEQ ID NOS:4559 and 4560, respectively). In addition, transmembrane prediction programs were run to determine whether or not the Pn1510 protein may contain a transmembrane domain. Analysis of the Pn1510P-278 and Pn1510P-243 amino acid sequences using the PSORT and PSORTII programs
20 revealed no potential transmembrane domains. However, analysis of these 2 protein sequences using a transmembrane prediction program identified a stretch of 20 hydrophobic amino acids, suggesting a possible transmembrane domain. This transmembrane domain occurs at amino acids 233-252 of the Pn1510P-278 ORF and at amino acids 198-217 of the Pn1510P-243 ORF.

25

EXAMPLE 12

SYNTHESIS OF PEPTIDES

Polypeptides are synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using FMOC chemistry with HPTU (O-
30 Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence is attached to the amino terminus of the peptide to provide a method

of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support is carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides are precipitated in cold methyl-t-butyl-ether. The 5 peptide pellets are then dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) is used to elute the peptides. Following lyophilization of the pure fractions, the peptides are characterized using electrospray or other types of mass spectrometry and by amino acid 10 analysis.

EXAMPLE 13

PEPTIDE PRIMING OF T-HELPER LINES

Generation of CD4⁺ T helper lines and identification of peptide epitopes 15 derived from tumor-specific antigens that are capable of being recognized by CD4⁺ T cells in the context of HLA class II molecules, is carried out as follows: Fifteen-mer peptides overlapping by 10 amino acids, derived from a tumor-specific antigen, are generated using standard procedures. Dendritic cells (DC) are derived from PBMC of a normal donor using GM-CSF and IL-4 by standard protocols. CD4⁺ T cells 20 are generated from the same donor as the DC using MACS beads (Miltenyi Biotec, Auburn, CA) and negative selection. DC are pulsed overnight with pools of the 15-mer peptides, with each peptide at a final concentration of 0.25 µg/ml. Pulsed DC are washed and plated at 1 x 10⁴ cells/well of 96-well V-bottom plates and purified CD4⁺ T cells are added at 1 x 10⁵/well. Cultures are supplemented with 60 ng/ml IL-6 and 10 25 ng/ml IL-12 and incubated at 37°C. Cultures are restimulated as above on a weekly basis using DC generated and pulsed as above as antigen presenting cells, supplemented with 5 ng/ml IL-7 and 10 U/ml IL-2. Following 4 *in vitro* stimulation cycles, resulting CD4⁺ T cell lines (each line corresponding to one well) are tested for specific proliferation and cytokine production in response to the stimulating pools of peptide 30 with an irrelevant pool of peptides used as a control.

EXAMPLE 14GENERATION OF TUMOR-SPECIFIC CTL LINES USING IN VITRO WHOLE-
GENE PRIMING

Using *in vitro* whole-gene priming with tumor antigen-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines are derived that specifically recognize autologous fibroblasts transduced with a specific tumor antigen, as determined by interferon- γ ELISPOT analysis. Specifically, dendritic cells (DC) are differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI 10 medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC are infected overnight with tumor antigen-recombinant vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μ g/ml CD40 ligand. Virus is then inactivated by UV irradiation. CD8+ T cells are isolated using a magnetic bead system, and priming cultures are initiated using standard culture techniques. Cultures are restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with previously identified tumor antigens. Following four stimulation cycles, CD8+ T cell lines are identified that specifically produce interferon- γ when stimulated with tumor antigen-transduced autologous fibroblasts. Using a panel of HLA-mismatched B-LCL lines transduced 20 with a vector expressing a tumor antigen, and measuring interferon- γ production by the CTL lines in an ELISPOT assay, the HLA restriction of the CTL lines is determined.

EXAMPLE 15GENERATION AND CHARACTERIZATION OF ANTI-TUMOR ANTIGEN
MONOCLONAL ANTIBODIES

25 Mouse monoclonal antibodies are raised against *E. coli* derived tumor antigen proteins as follows: Mice are immunized with Complete Freund's Adjuvant (CFA) containing 50 μ g recombinant tumor protein, followed by a subsequent intraperitoneal boost with Incomplete Freund's Adjuvant (IFA) containing 10 μ g recombinant protein. Three days prior to removal of the spleens, the mice are 30 immunized intravenously with approximately 50 μ g of soluble recombinant protein.

The spleen of a mouse with a positive titer to the tumor antigen is removed, and a single-cell suspension made and used for fusion to SP2/O myeloma cells to generate B cell hybridomas. The supernatants from the hybrid clones are tested by ELISA for specificity to recombinant tumor protein, and epitope mapped using peptides that 5 spanned the entire tumor protein sequence. The mAbs are also tested by flow cytometry for their ability to detect tumor protein on the the surface of cells stably transfected with the cDNA encoding the tumor protein.

From the foregoing it will be appreciated that, although specific 10 embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

What is Claimed:

1. An isolated polynucleotide comprising a sequence selected from the group consisting of:
 - (a) sequences provided in SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550;
 - (b) complements of the sequences provided in SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550;
 - (c) sequences consisting of at least 20 contiguous residues of a sequence provided in SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550;
 - (d) sequences that hybridize to a sequence provided in SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550, under moderately stringent conditions;
 - (e) sequences having at least 75% identity to a sequence of SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550;
 - (f) sequences having at least 90% identity to a sequence of SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550; and
 - (g) degenerate variants of a sequence provided in SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550.
2. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:
 - (a) sequences encoded by a polynucleotide of claim 1;
 - (b) sequences having at least 70% identity to a sequence encoded by a polynucleotide of claim 1;
 - (c) sequences having at least 90% identity to a sequence encoded by a polynucleotide of claim 1; and

- (d) a polypeptide sequence set forth in SEQ ID NOs: SEQ ID NOs:67-74, 153-173, 178-181, 183, 453, 4551-4554, 4558-4560;
- (e) sequences having at least 70% identity to a polypeptide sequence set forth in SEQ ID NOs:67-74, 153-173, 178-181, 183, 453, 4551-4554, 4558-4560; and
- (f) sequences having at least 90% identity to a polypeptide sequence set forth in SEQ ID NOs:67-74, 153-173, 178-181, 183, 453, 4551-4554, 4558-4560.

3. An expression vector comprising a polynucleotide of claim 1 operably linked to an expression control sequence.

4. A host cell transformed or transfected with an expression vector according to claim 3.

5. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a polypeptide of claim 2.

6. A method for detecting the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with a binding agent that binds to a polypeptide of claim 2;
- (c) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (d) comparing the amount of polypeptide to a predetermined cut-off value and therefrom determining the presence of a cancer in the patient.

7. A fusion protein comprising at least one polypeptide according to claim 2.

8. An oligonucleotide that hybridizes to a sequence recited in SEQ ID NOs:1-66, 75-152, 174-177, 182, 184-452, and 454-4550 under moderately stringent conditions.

9. A method for stimulating and/or expanding T cells specific for a tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1; and
- (c) antigen-presenting cells that express a polypeptide according to claim 2,

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

10. An isolated T cell population, comprising T cells prepared according to the method of claim 9.

11. A composition comprising a first component selected from the group consisting of physiologically acceptable carriers and immunostimulants, and a second component selected from the group consisting of:

- (a) polypeptides according to claim 2;
- (b) polynucleotides according to claim 1;
- (c) antibodies according to claim 5;
- (d) fusion proteins according to claim 7;
- (e) T cell populations according to claim 10; and
- (f) antigen presenting cells that express a polypeptide according to claim 2.

12. A method for stimulating an immune response in a patient, comprising administering to the patient a composition of claim 11.

13. A method for the treatment of a pancreatic cancer in a patient, comprising administering to the patient a composition of claim 11.

14. A method for determining the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with an oligonucleotide according to claim 8;
- (c) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (d) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence of the cancer in the patient.

15. A diagnostic kit comprising at least one oligonucleotide according to claim 8.

16. A diagnostic kit comprising at least one antibody according to claim 5 and a detection reagent, wherein the detection reagent comprises a reporter group.

17. A method for inhibiting the development of a cancer in a patient, comprising the steps of:

- (a) incubating CD4+ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of: (i) polypeptides according to claim 2; (ii) polynucleotides according to claim 1; and (iii) antigen presenting cells that express a polypeptide of claim 2, such that T cell proliferate;
 - (b) administering to the patient an effective amount of the proliferated T cells,
- and thereby inhibiting the development of a cancer in the patient.